

Fig. 1

Compound A

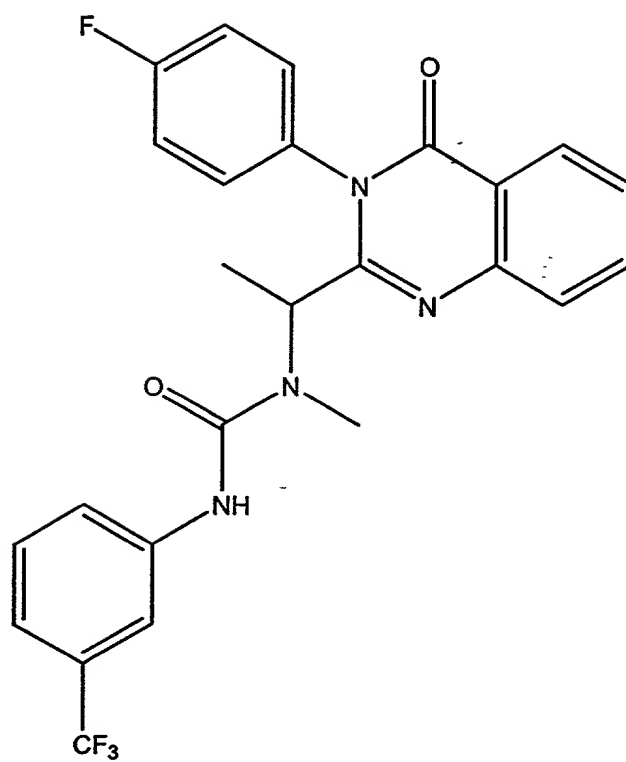


Fig. 2A

Compound B

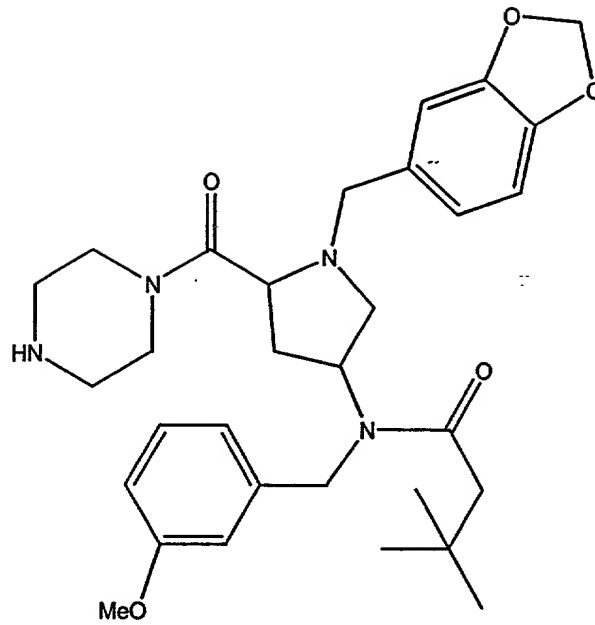
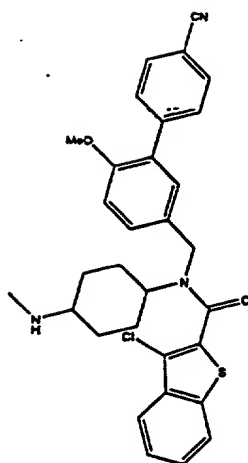


Fig. 2B



Agonist Z

Fig. 3



# **Gli-1, Gene Expression in the Lung**

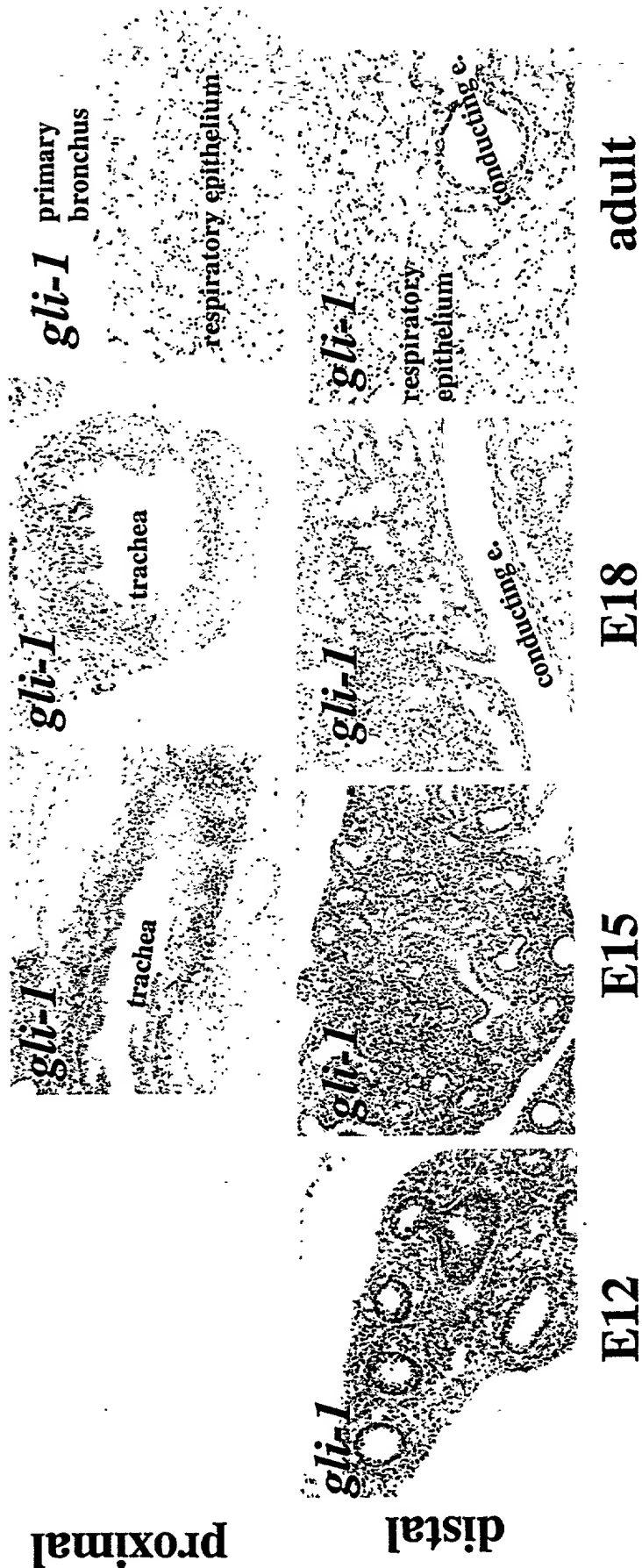


Fig. 4

# **Gli-1 expression is inversely related to lung maturation**

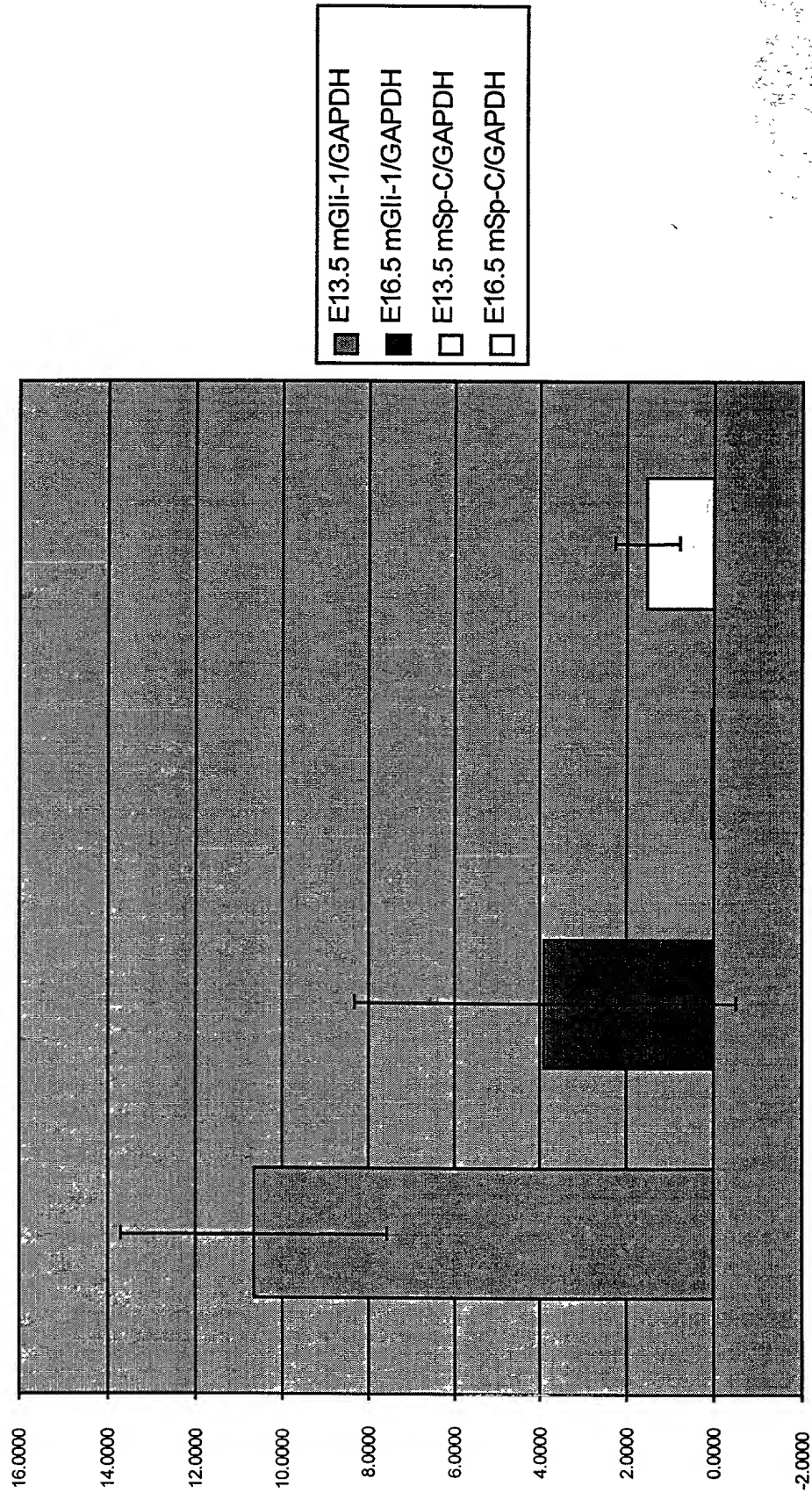


Fig. 5

FOSTER 19822560

# Compound B Downregulates mGli-1 in Lung Explant Cultures

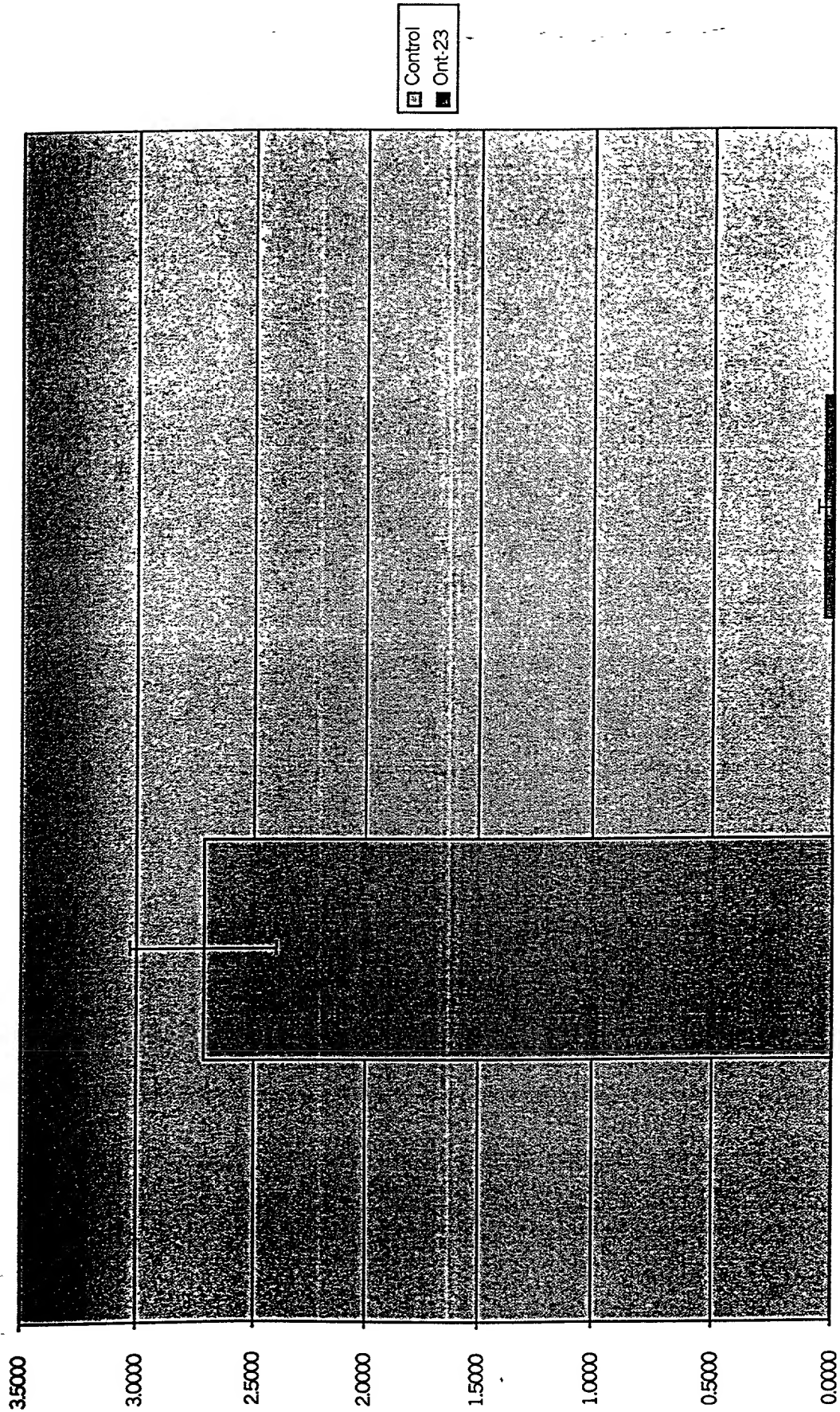


Fig. 6

# Compound B Treatment Increases Surfactant type C Production in Embryonic Mouse Lungs

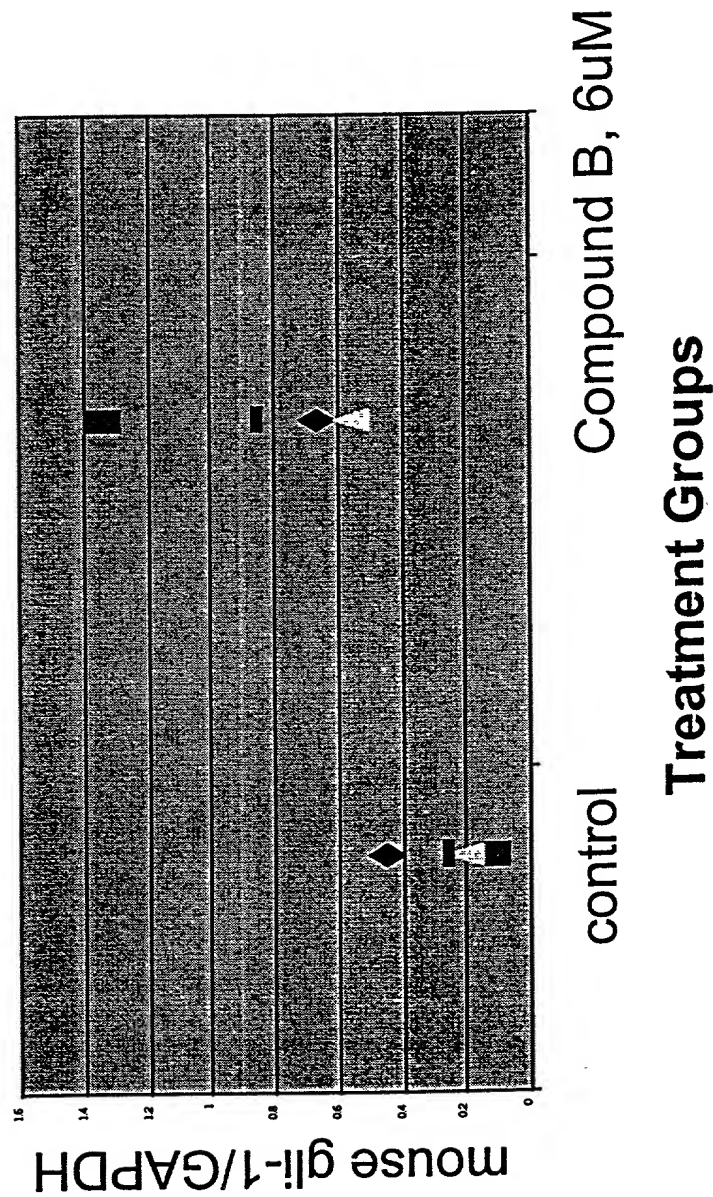
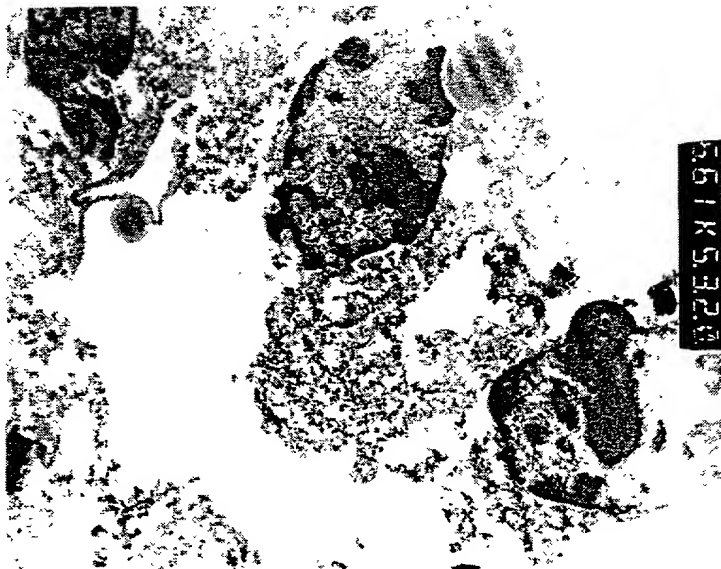


Fig. 7

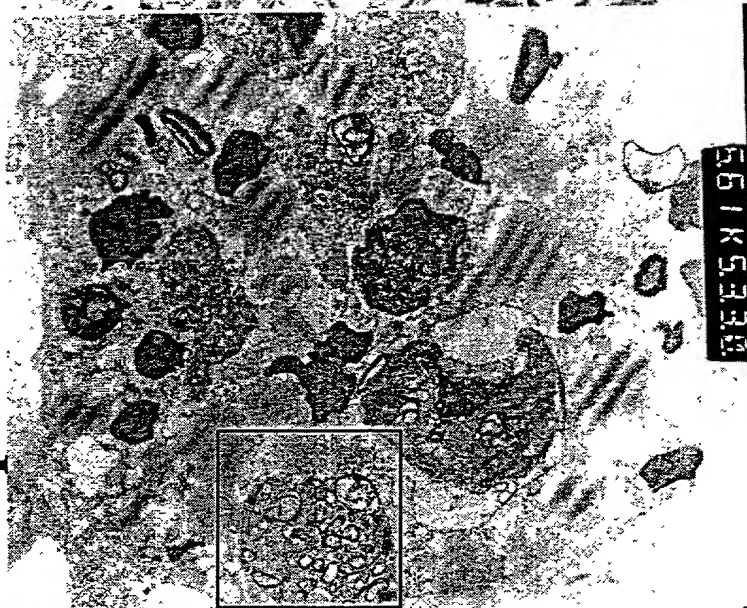


# Type II Pneumocytes in Compound B Treated Lung Cultures Differentiate Prematurely

vehicle



Compound B



Compound B, inset

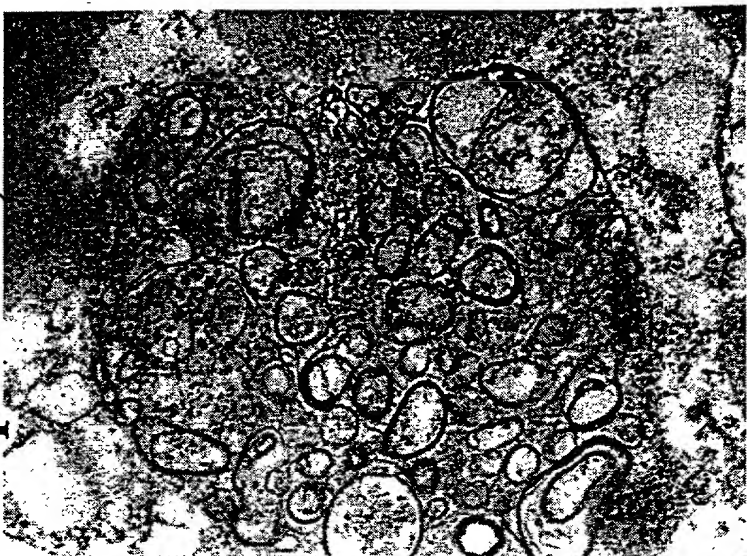


Fig. 8

FOOT 1982-83

## Compound B

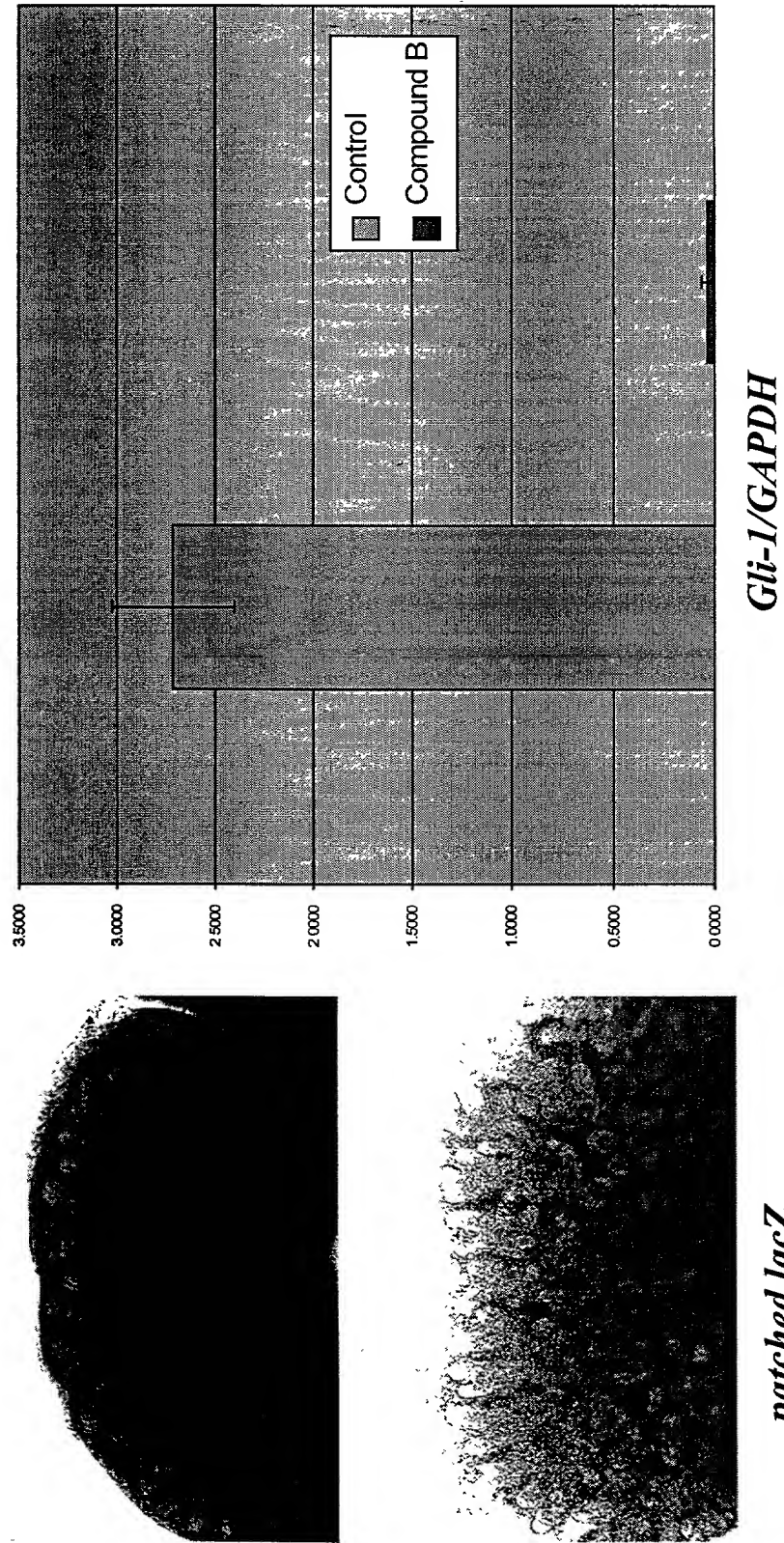


Fig. 9

# Compound B

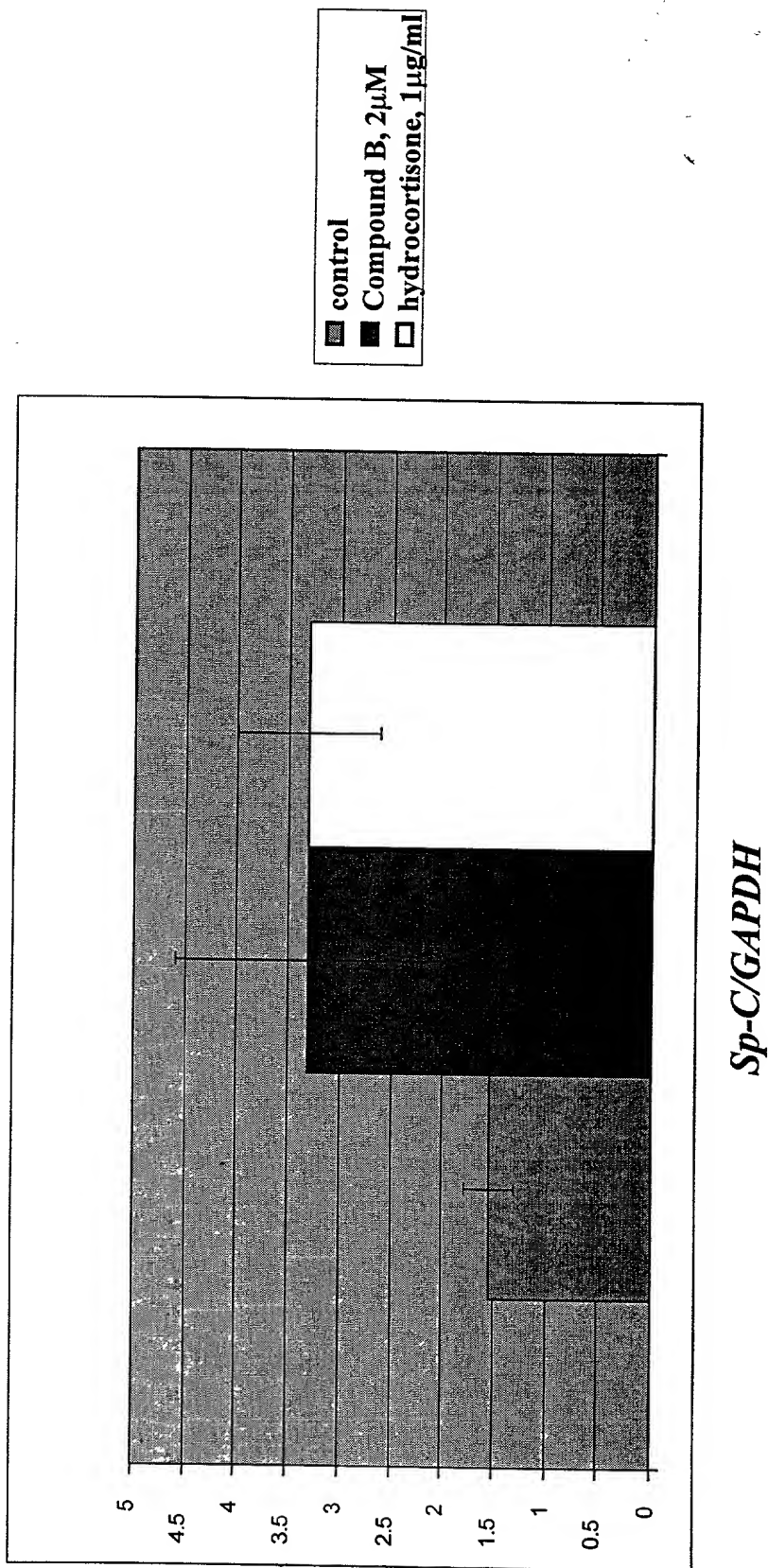


Fig. 10

# Shh Protein and Hedgehog Agonist Z

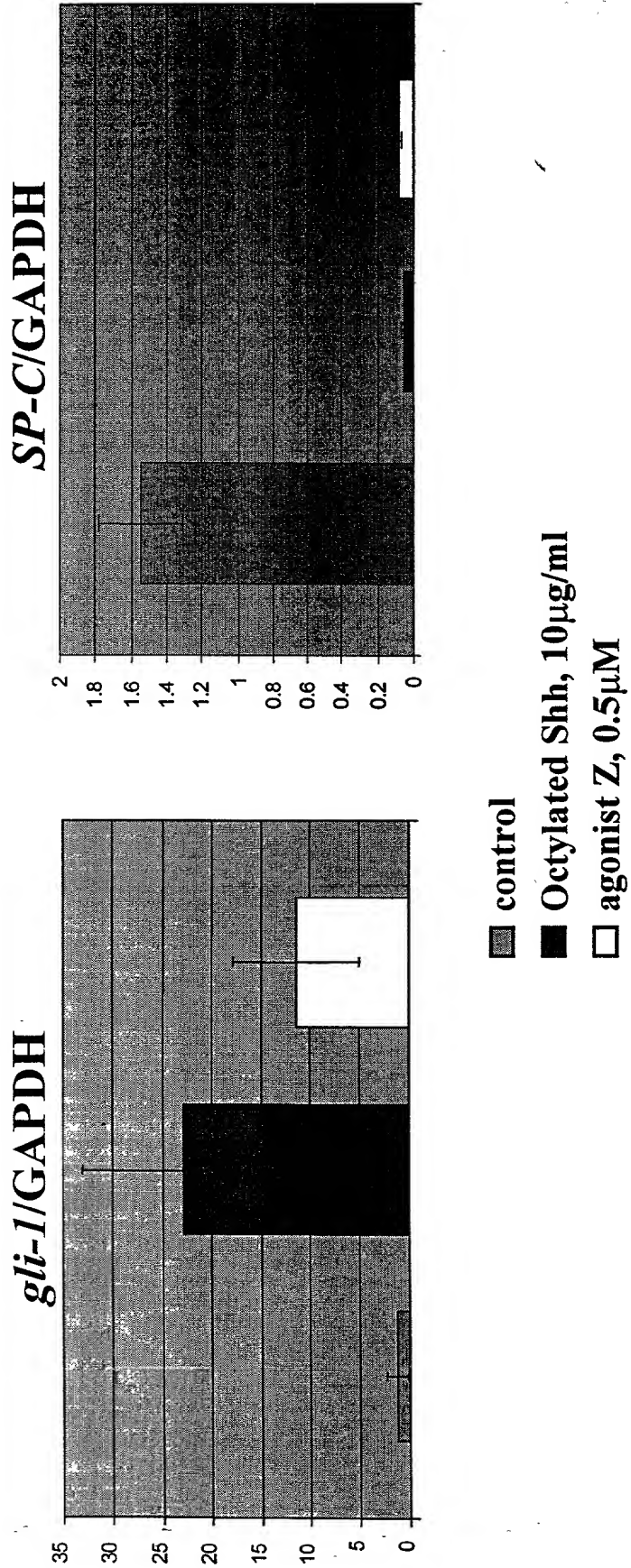


Fig. 11



105101-19822660

# Breast Cancer *Gli-1* In Situ Hybridization - Epithelial Expression

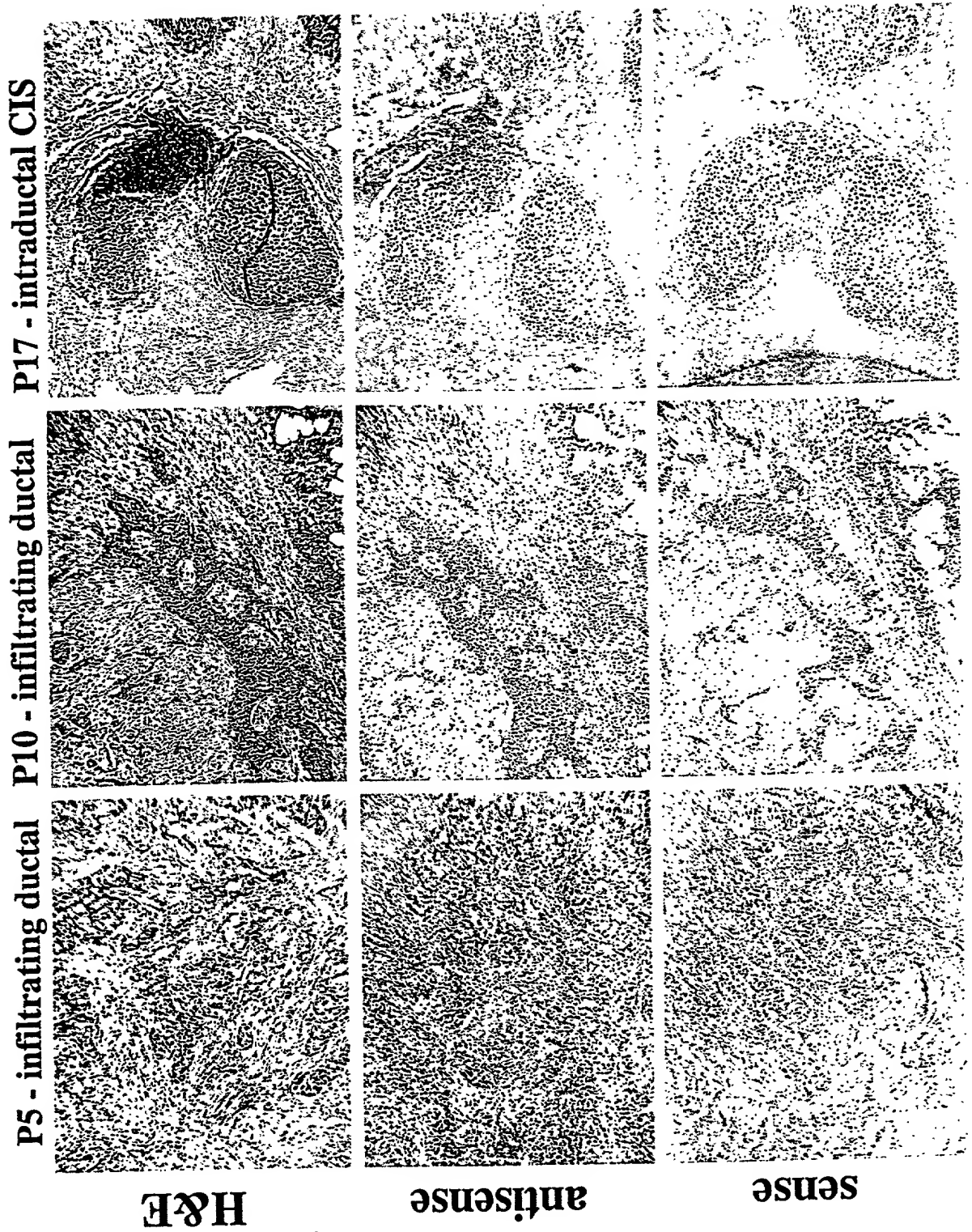


Fig. 12

# Lung Cancer *Gli-1* In Situ Hybridization

L4 - adenocarcinoma L17 - small cell carcinoma L20 - small cell carcinoma

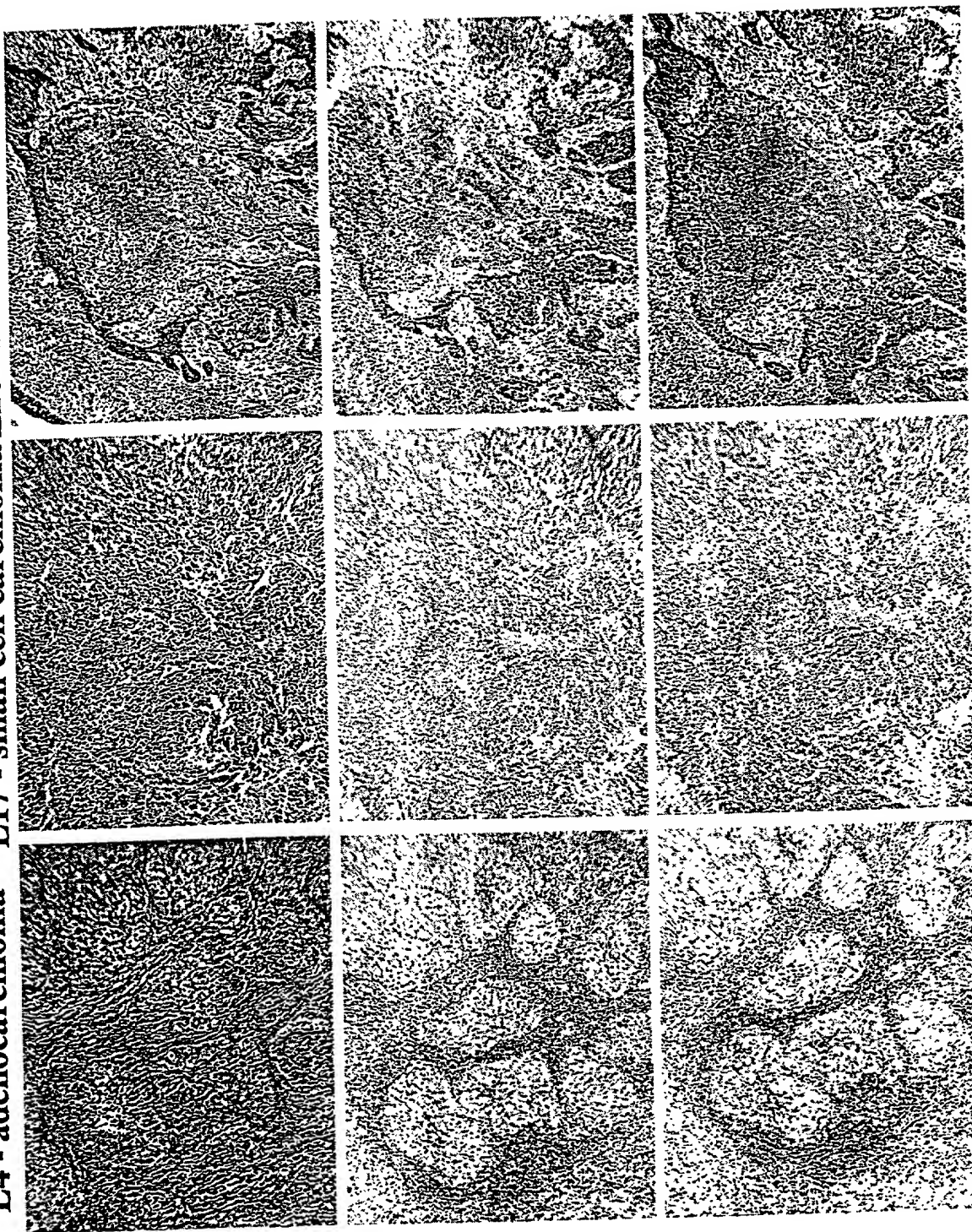
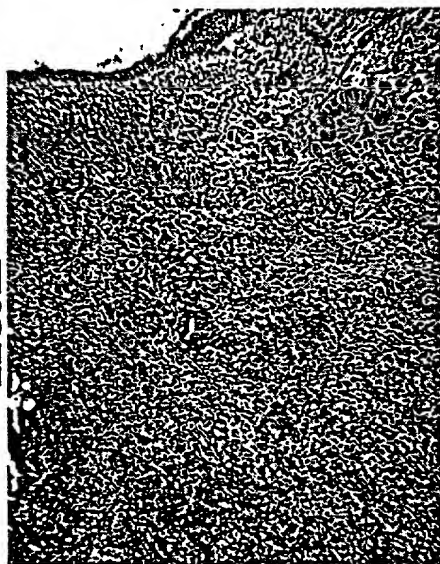


Fig. 13

# Prostate Cancer *Gli-1* In Situ Hybridization - Stromal Expression

H&E



antisense



sense



Fig. 14

FOOT 498266

# BPH *Gli-1* In Situ Hybridization - Stromal Expression

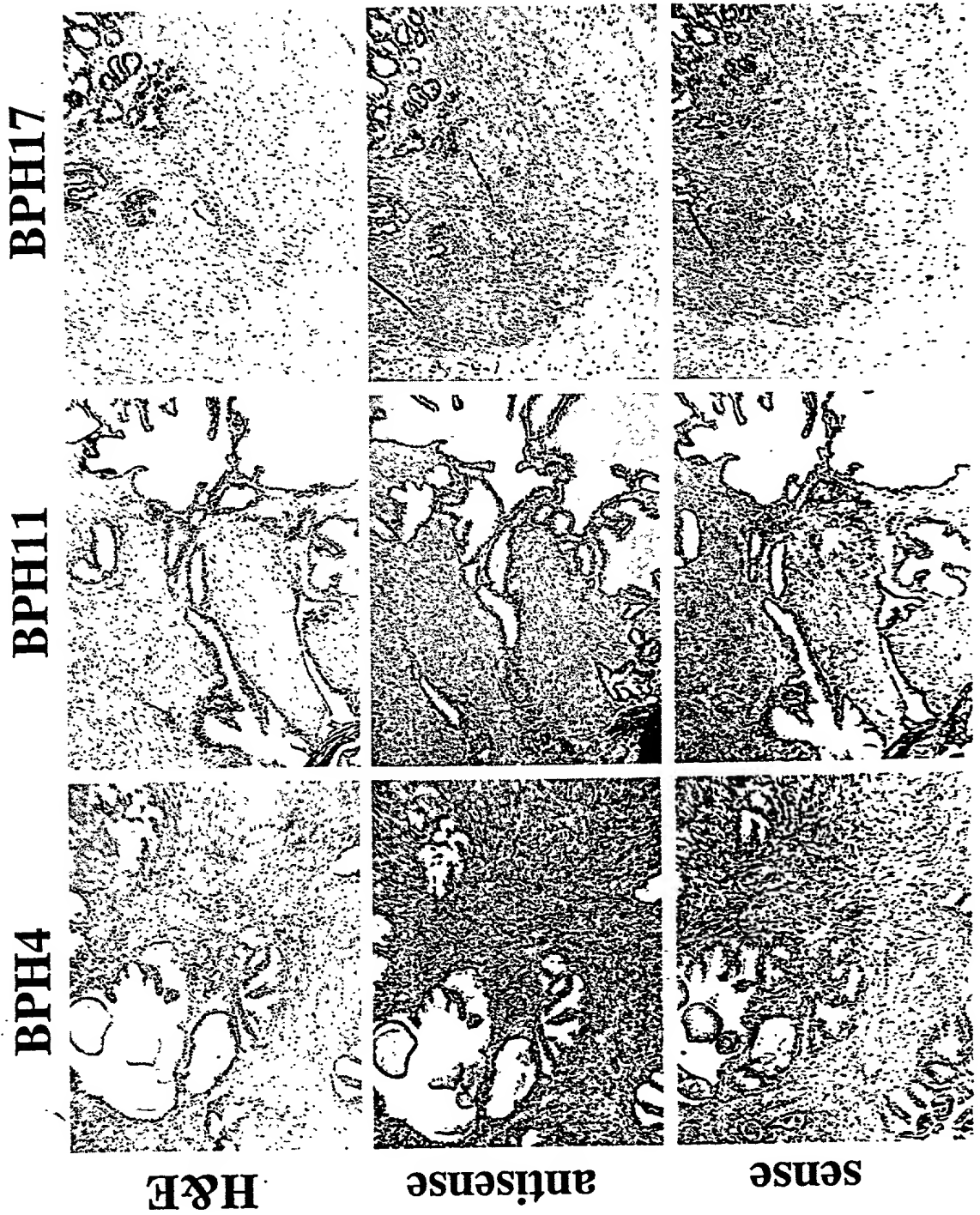


Fig. 15

# Hedgehog Signaling in Mouse Bladder

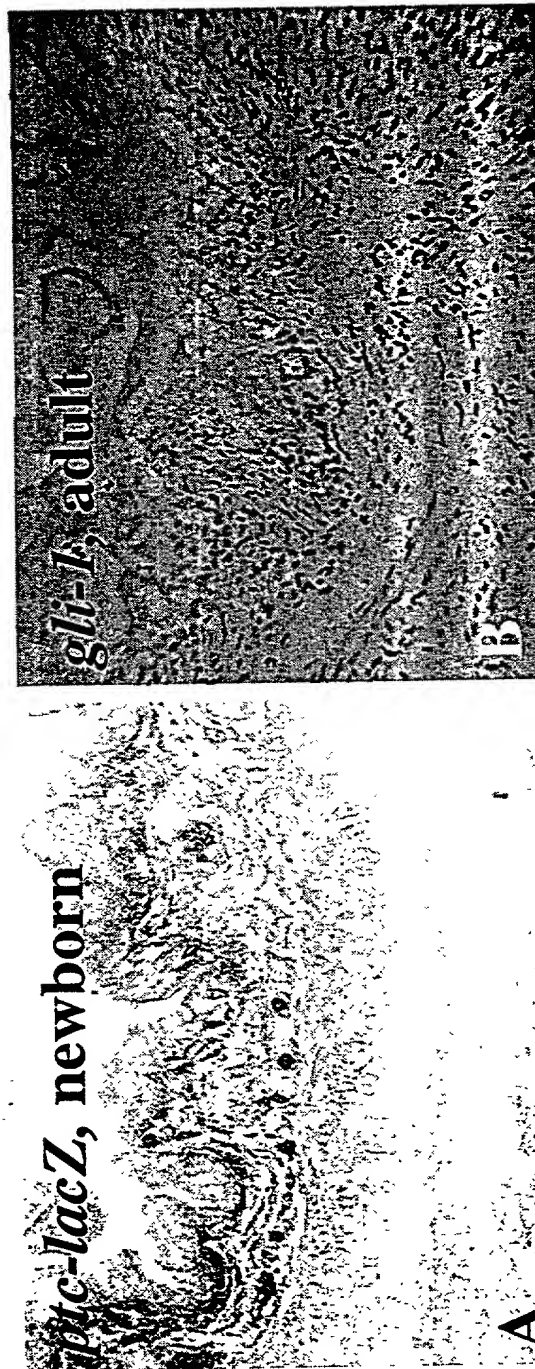


Fig. 16



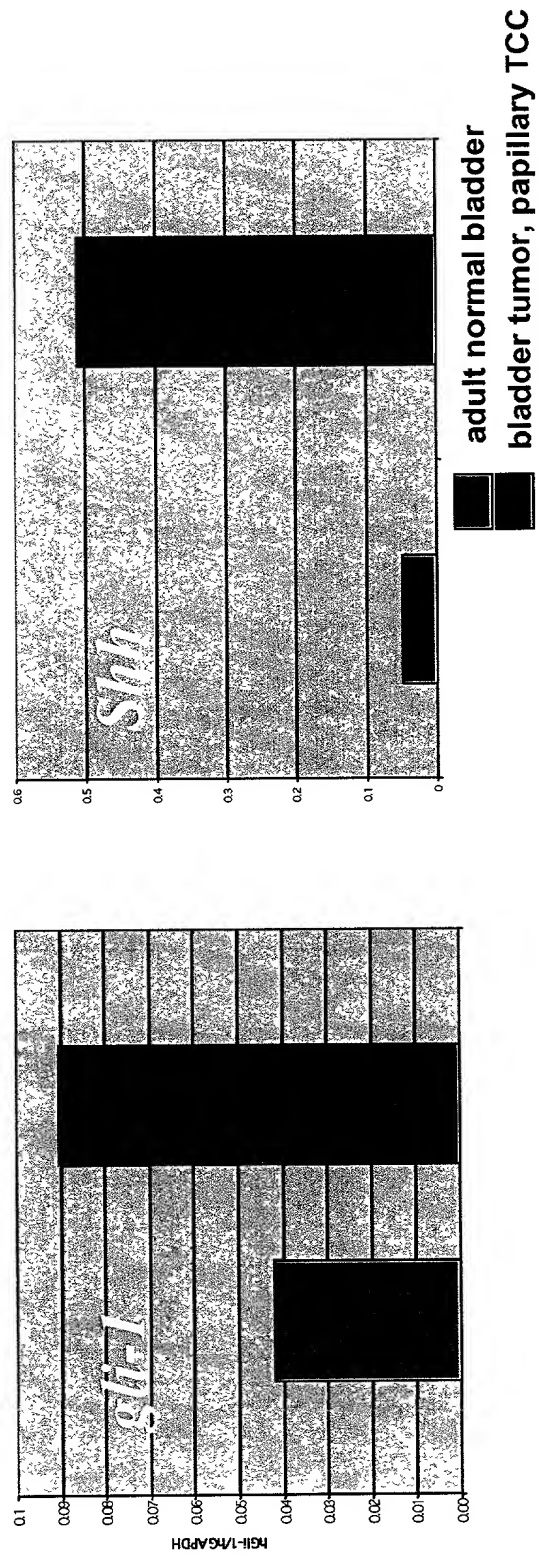


Fig. 17

# HH SIGNALING IN BLADDER CANCER CELL LINES

(1d in 10% FBS, 2d in 1% FBS)

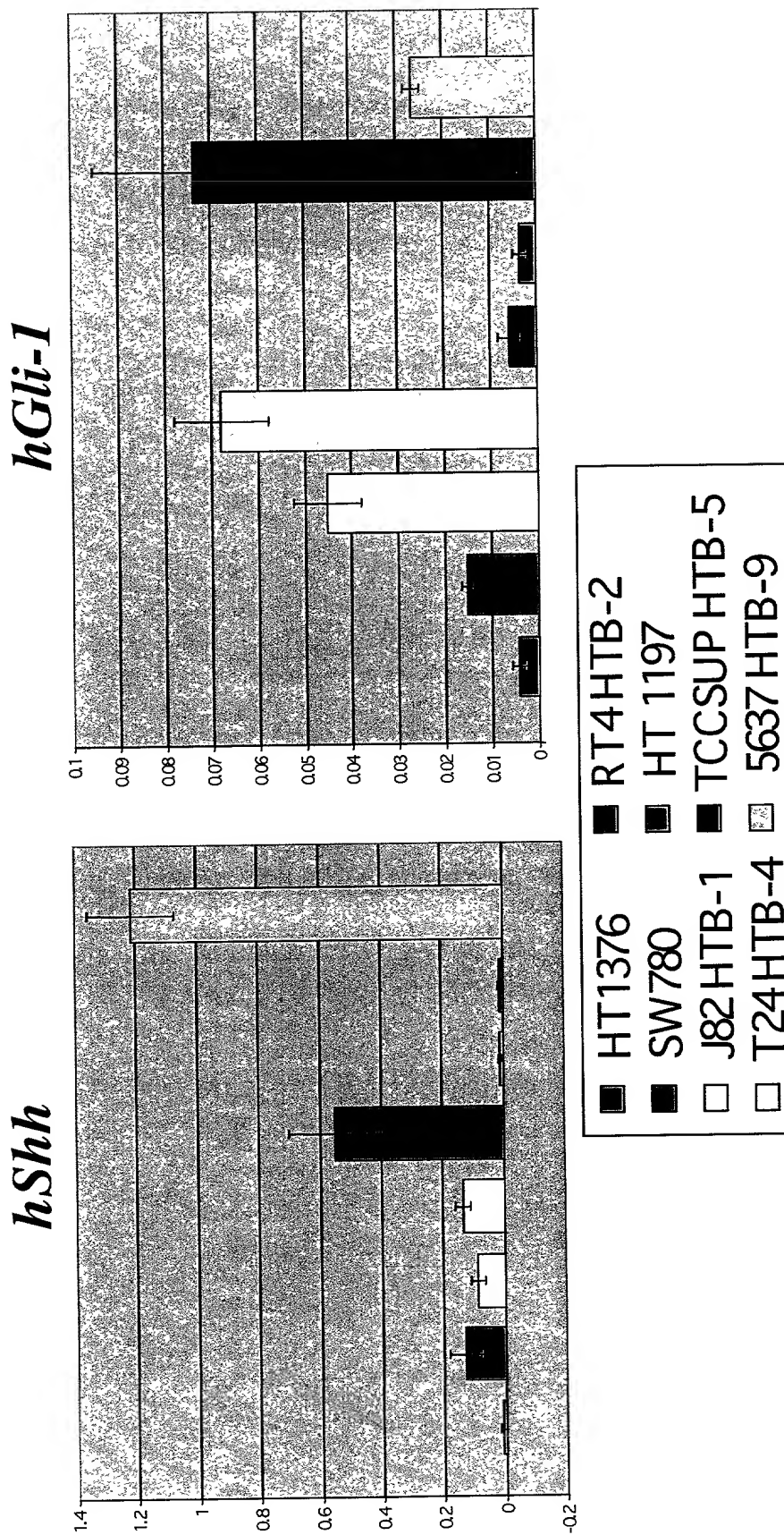


Fig. 18

# HH SIGNALING IN BLADDER CANCER CELL LINES

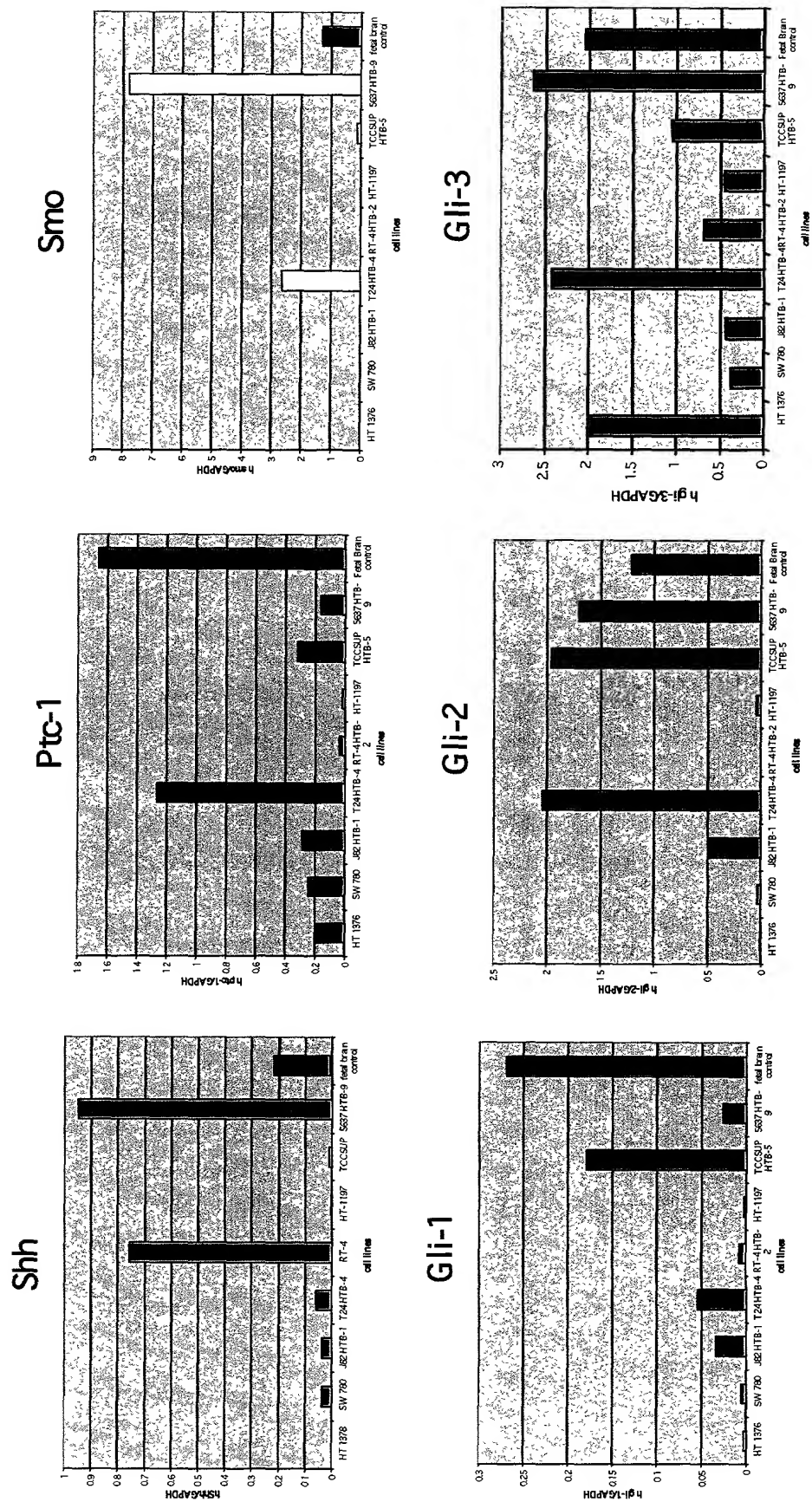


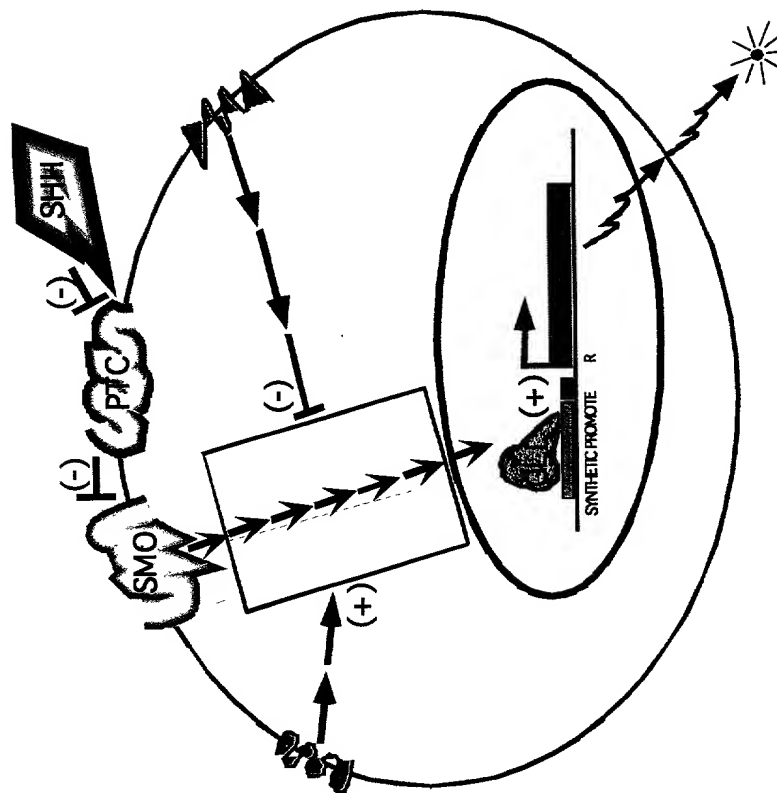
Fig. 19



# IN VITRO EFFICACY

## Gli-luc Assay

A. S12 fibroblast cell line with luciferase reporter



B. Flow-chart

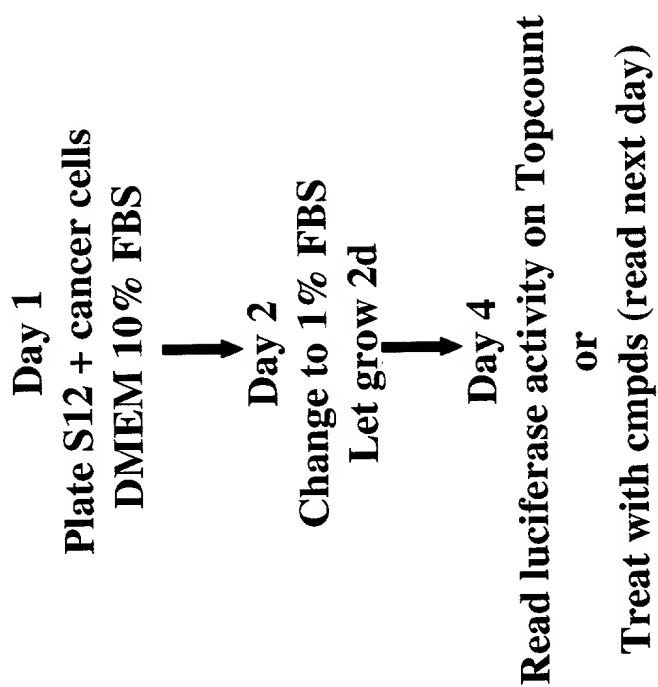


Fig. 20

# GLI-LUC ASSAY ON BLADDER CANCER CELL LINES

(S12 + cancer cell co-cultures, 1d in 10% FBS, 2d in 1% FBS)

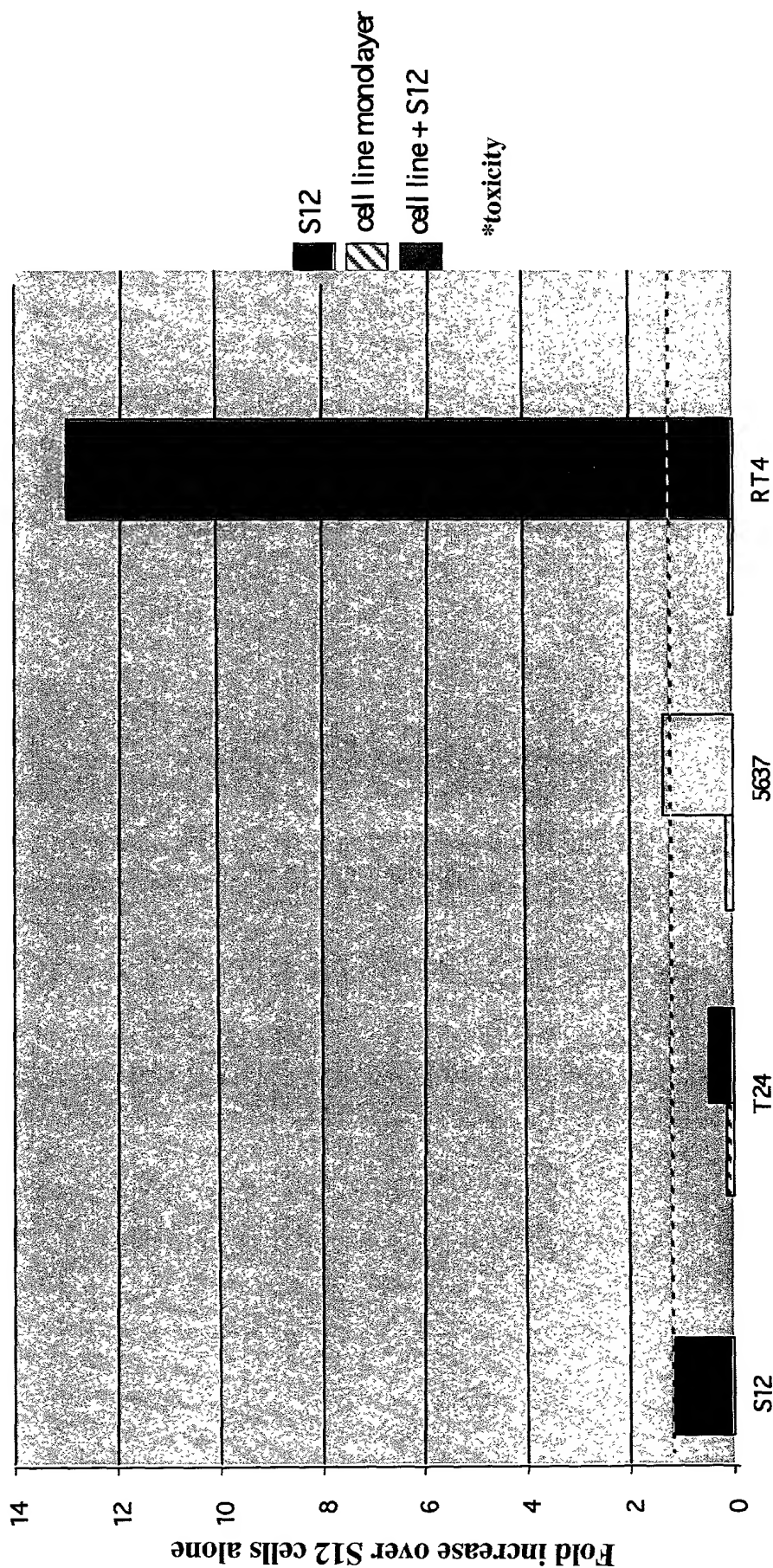
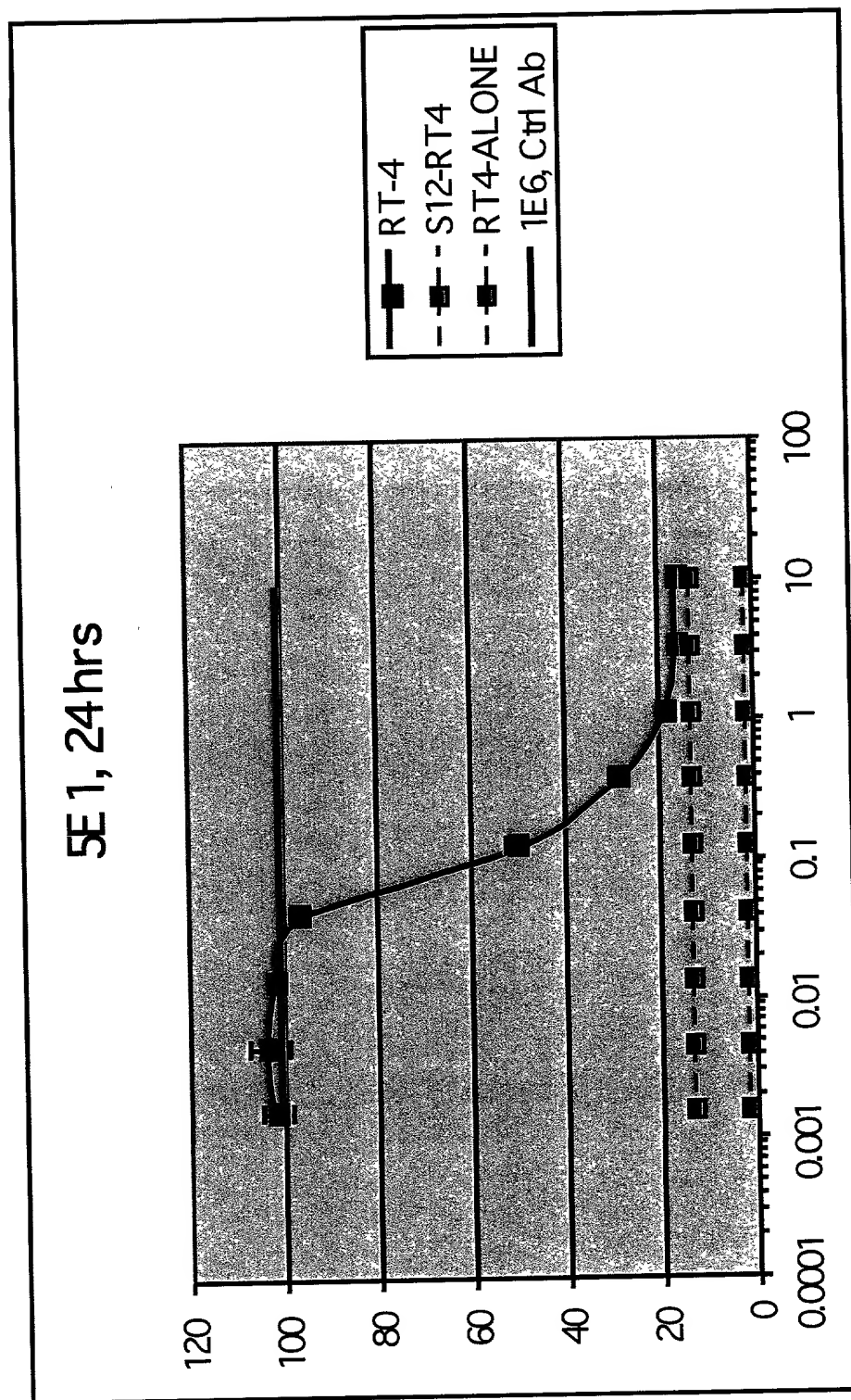


Fig. 21

# GLI-LUC ASSAY ON RT-4



IC<sub>50</sub>=85ng/ml IC<sub>90</sub>=500ng/ml

Fig. 22

# RT-4 IN VIVO EFFICACY EXPERIMENT

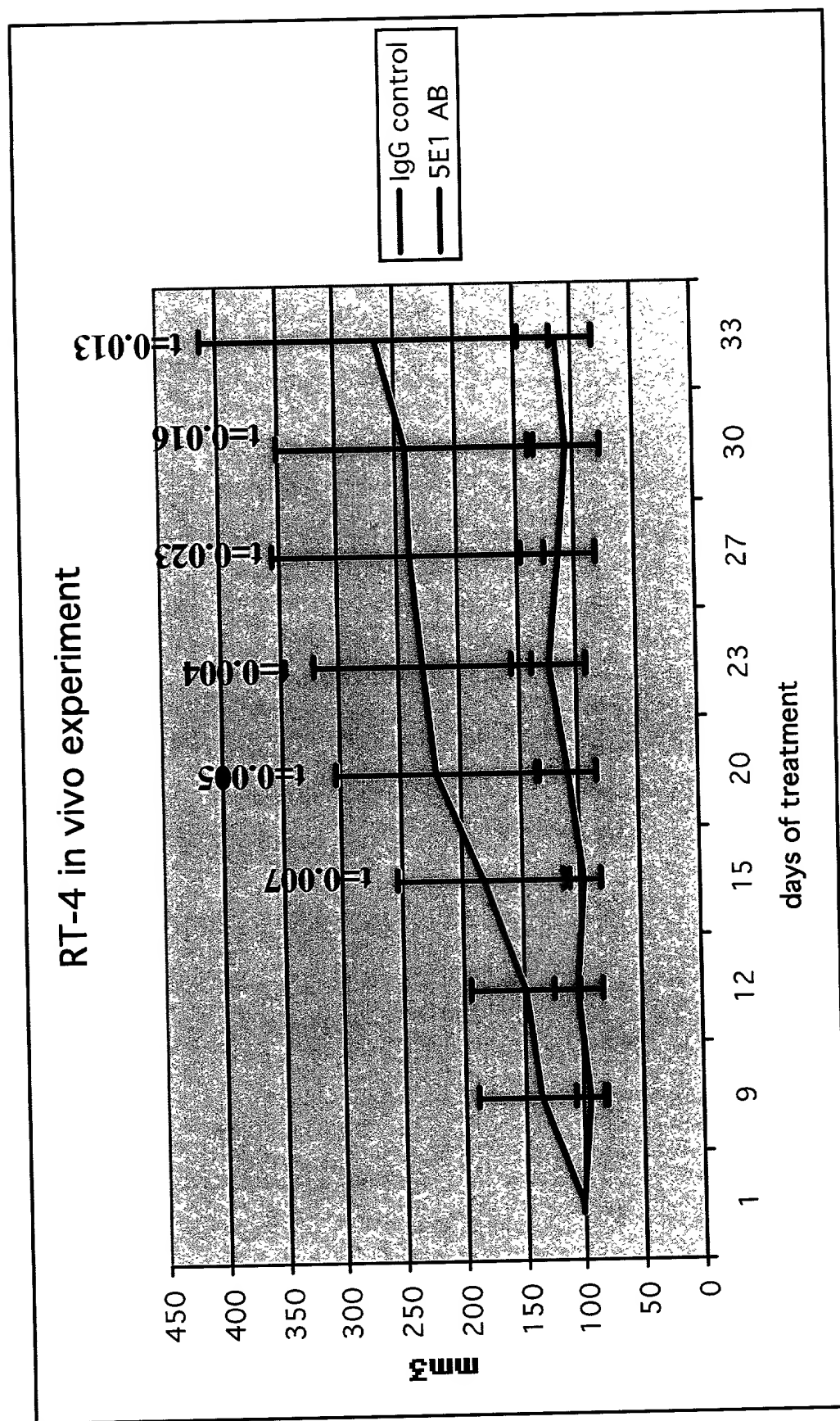
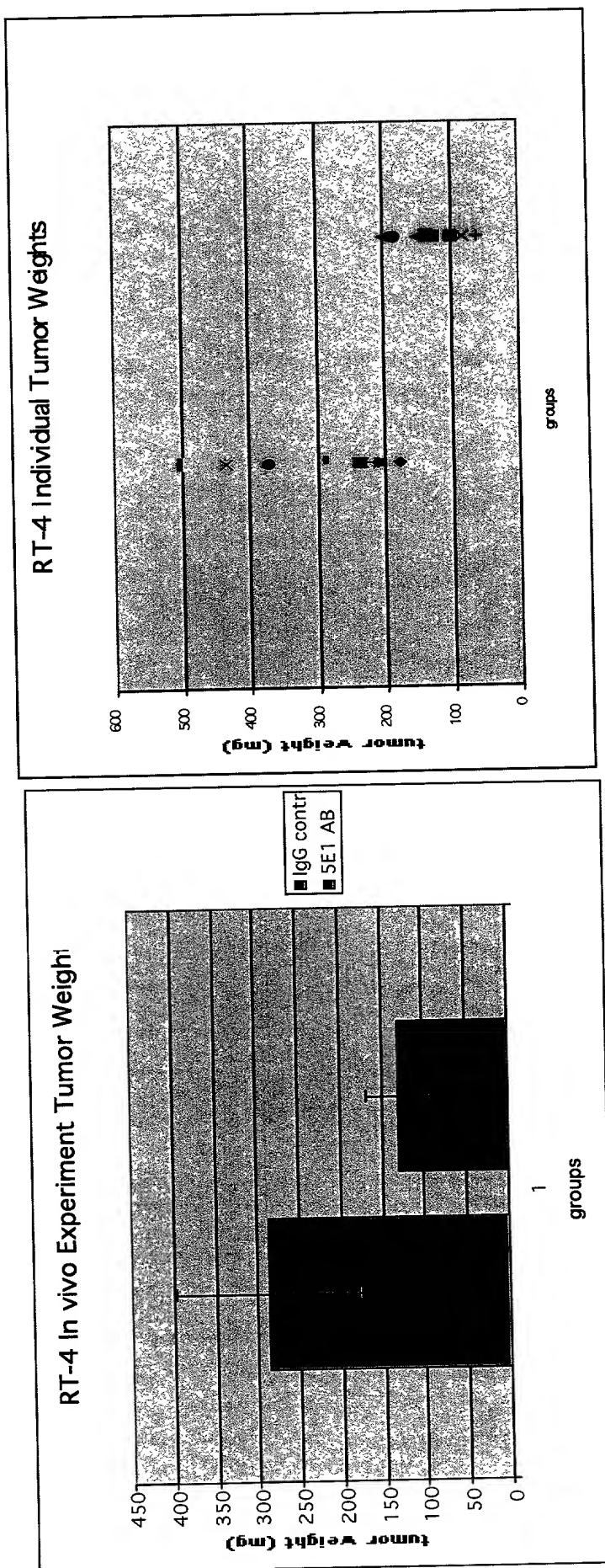
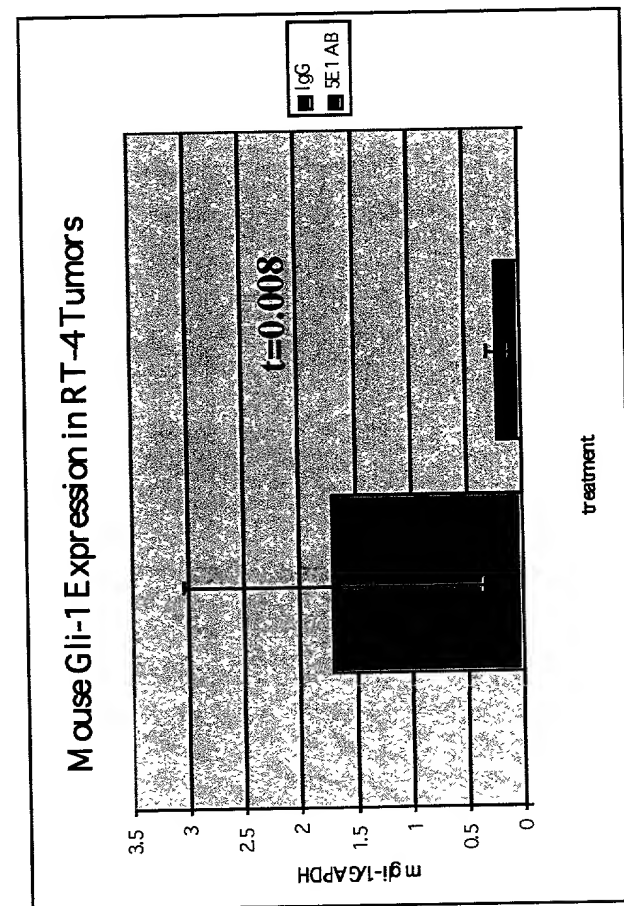


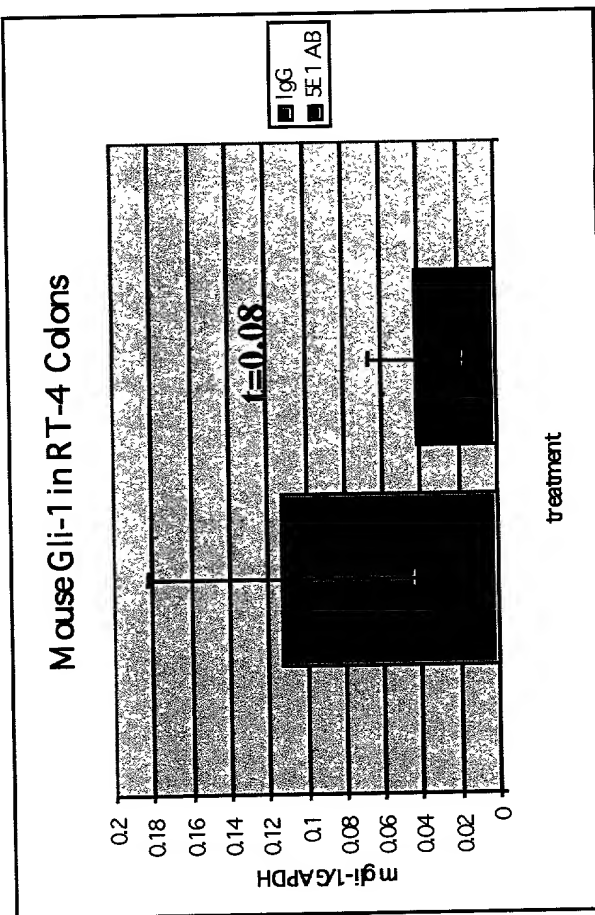
Fig. 23



# Mouse Gli-1 Expression in 5E1-Treated RT-4 Tumors



mouse small intestine standard = 0.06



mouse small intestine standard = 0.1

Fig. 25

# PROSTATE CANCER

*Shh* is Expressed in Prostate Cancer

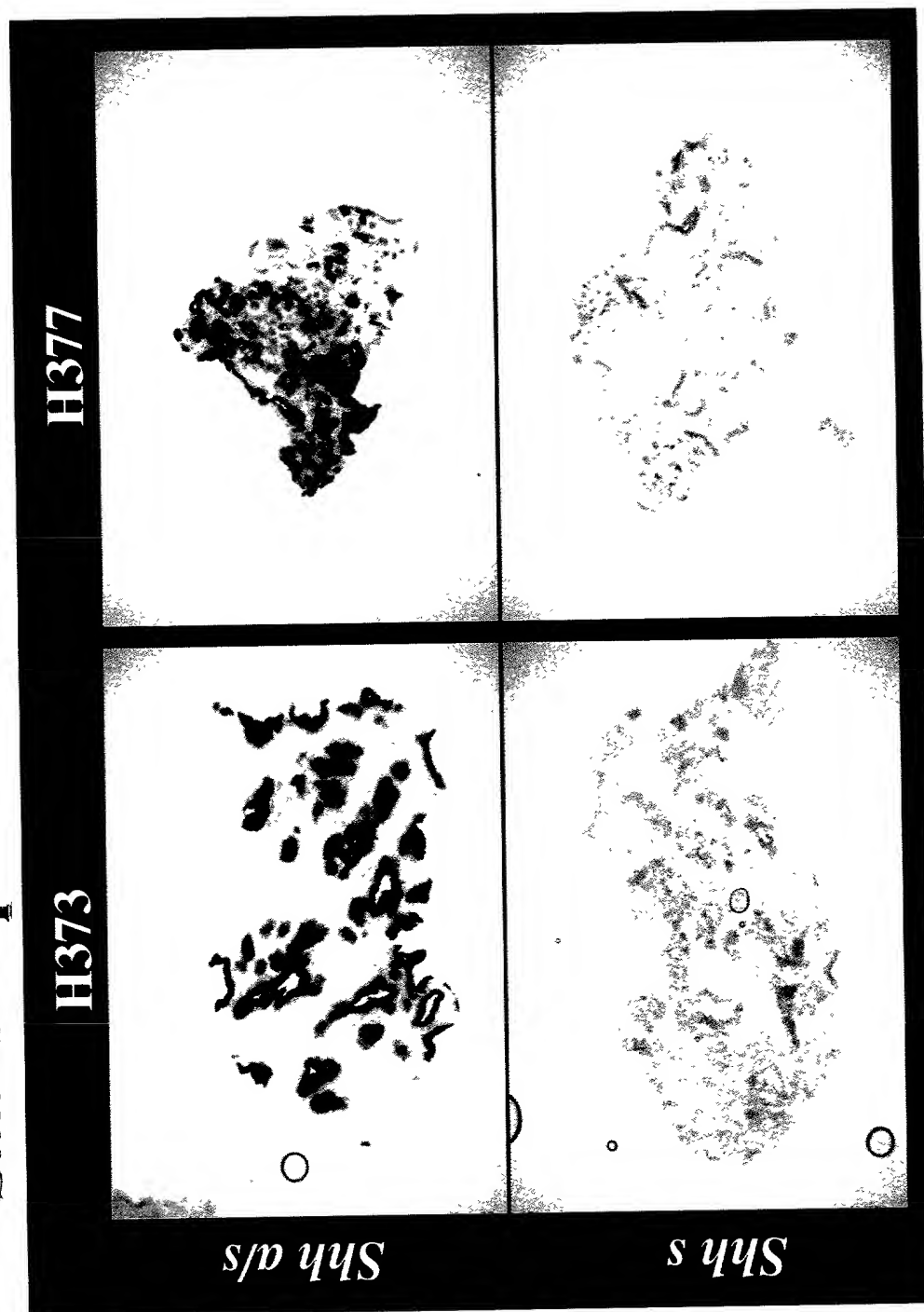


Fig. 26



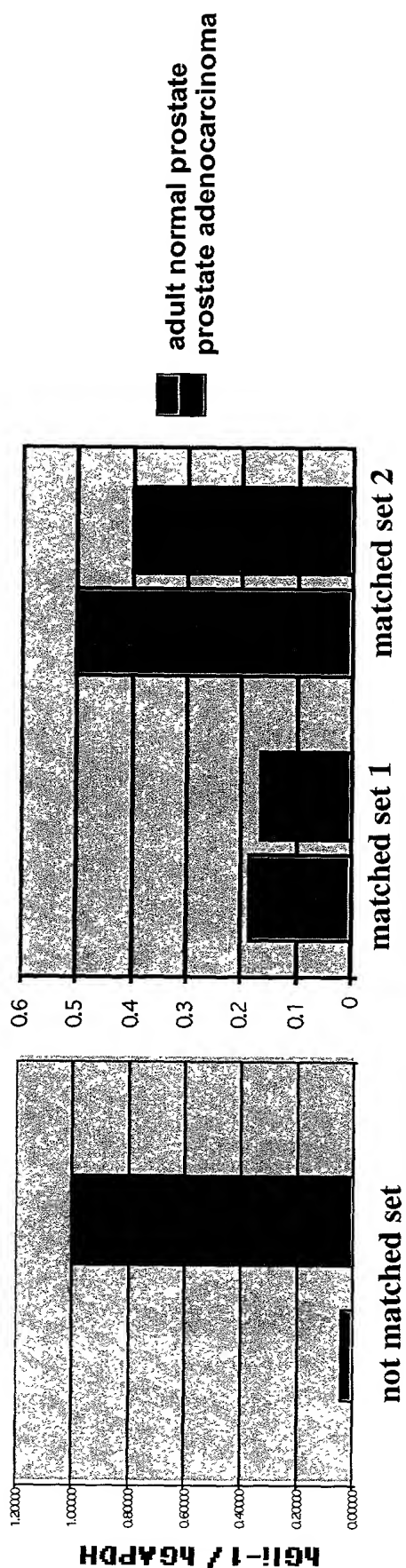


Fig. 27



# HH SIGNALING IN PROSTATE CANCER CELL LINES

(1d in 10% FBS, 2d in 1% FBS)

*hGli-1*

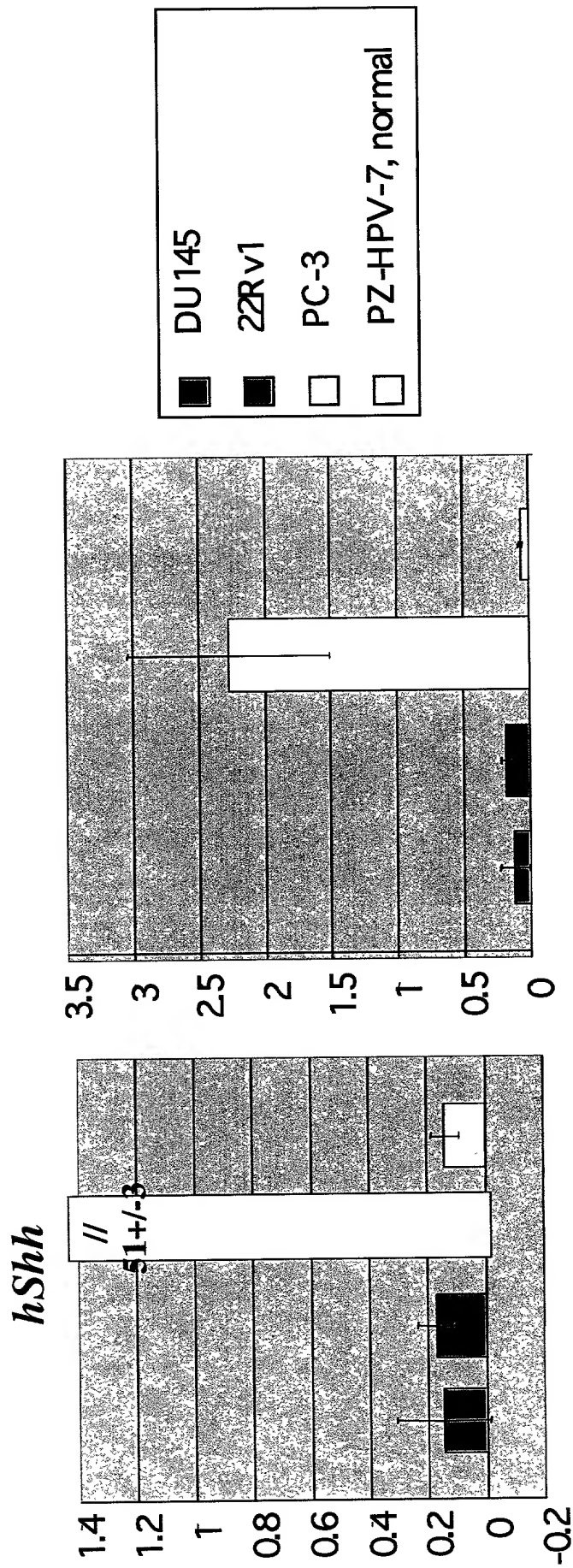


Fig. 28

# GLI-LUC ASSAY ON PROSTATE CANCER CELL LINES

(S12 + cancer cell co-cultures, 1d in 10% FBS, 2d in 1% FBS)

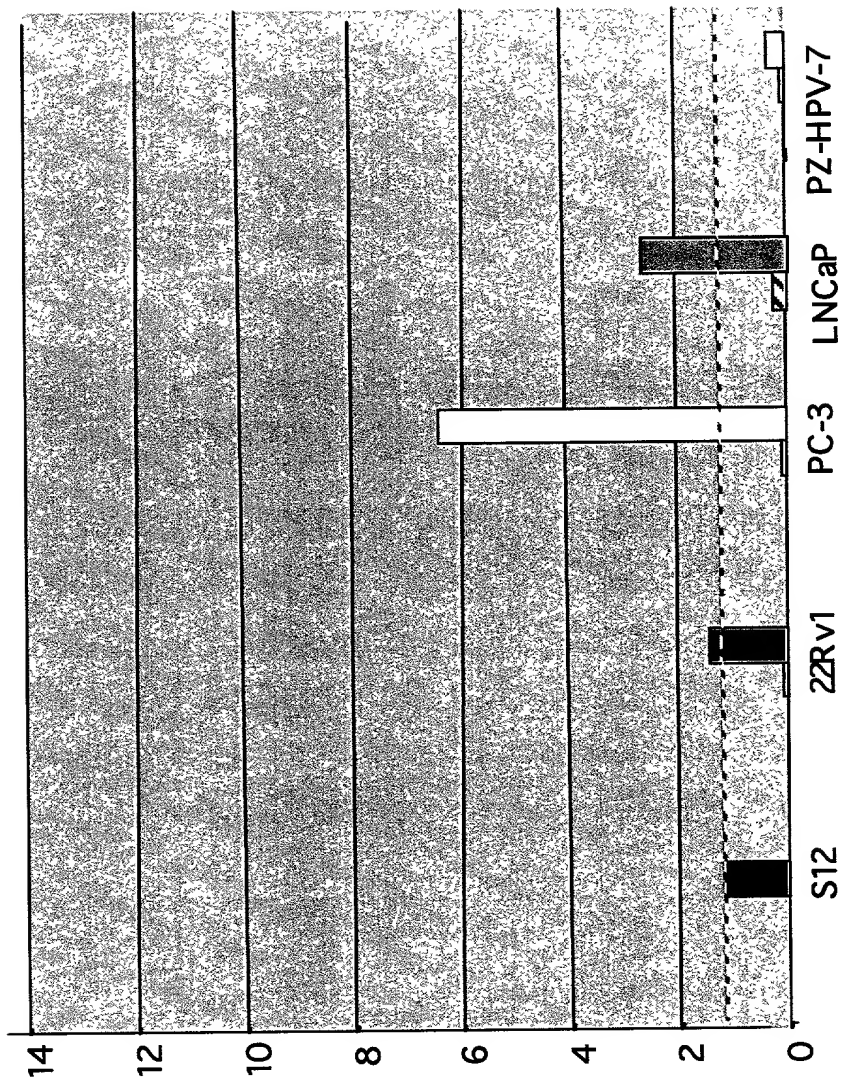


Fig. 29

# IN VITRO EFFICACY

Inhibition of hedgehog signaling by Hedgehog Antagonists  
(Gli-luc, 24 hrs)

5E1

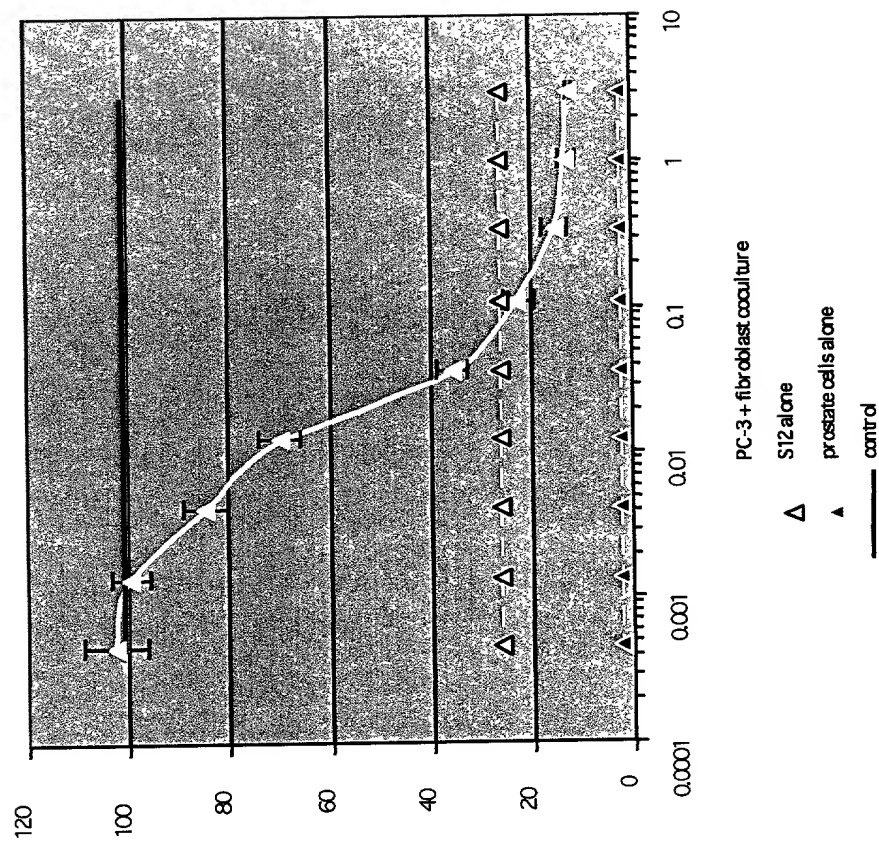


Fig. 30

# **Expression of *Shh* in the Prostatic Epithelium and Stroma**

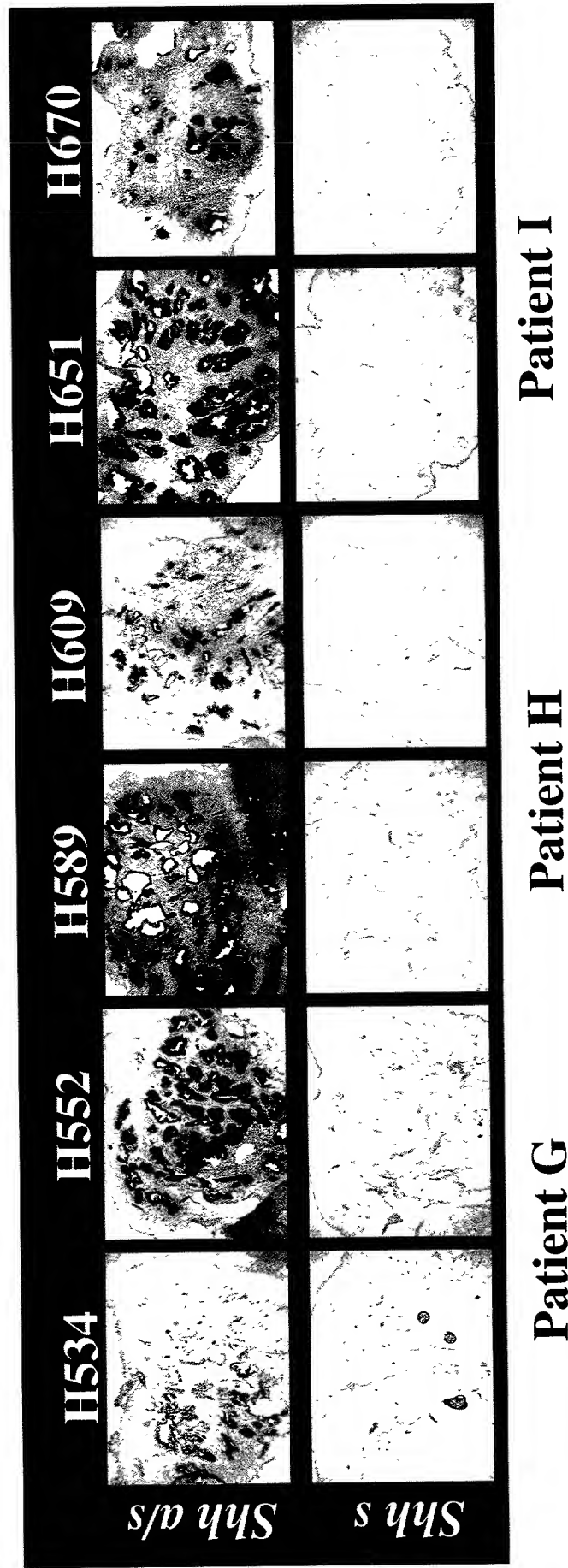


Fig. 31

## Expression of *Gli-1* in the Prostatic Stroma (LifeSpan)

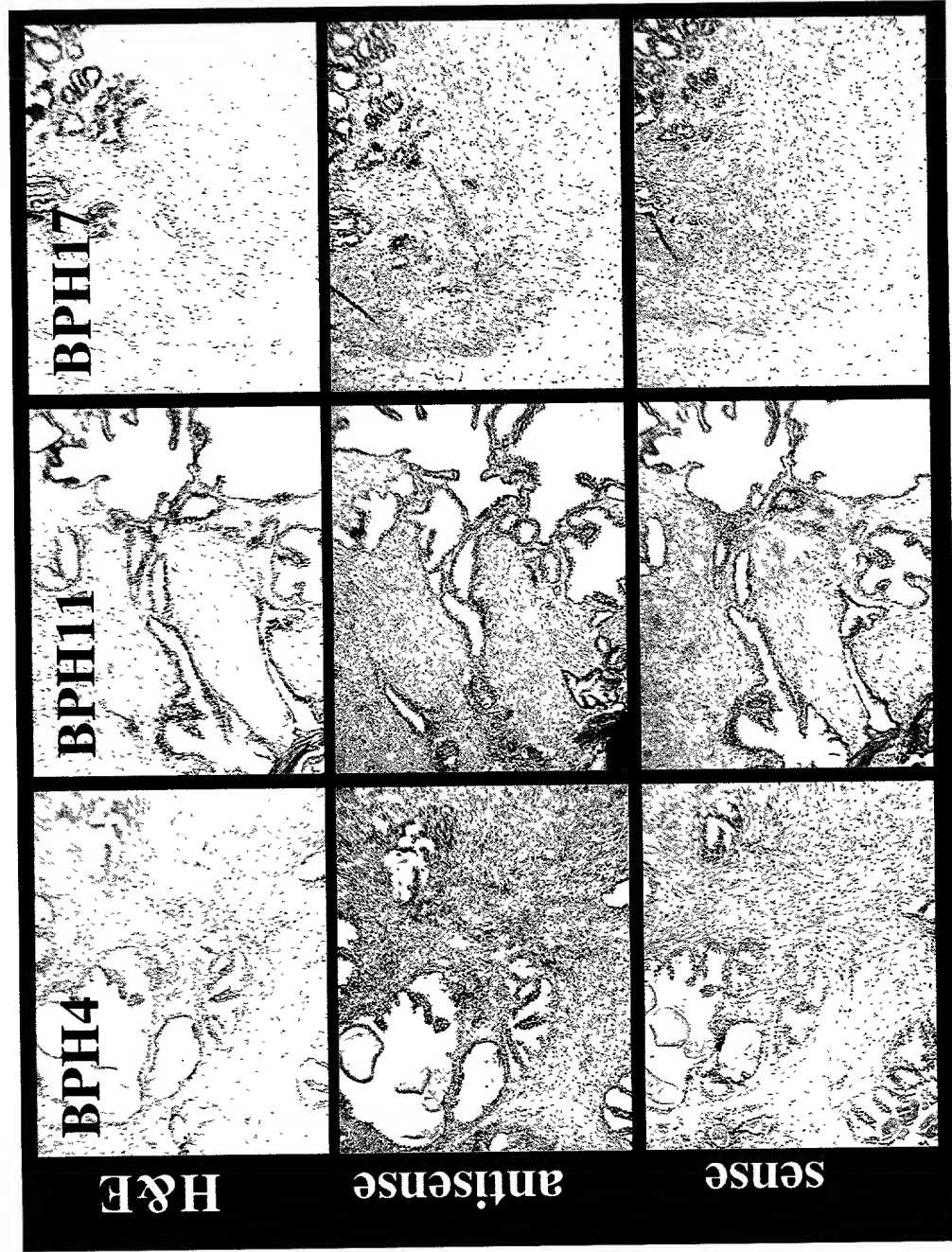


Fig. 32



## Proximo-Distal Shh Gradient in Normal Prostate

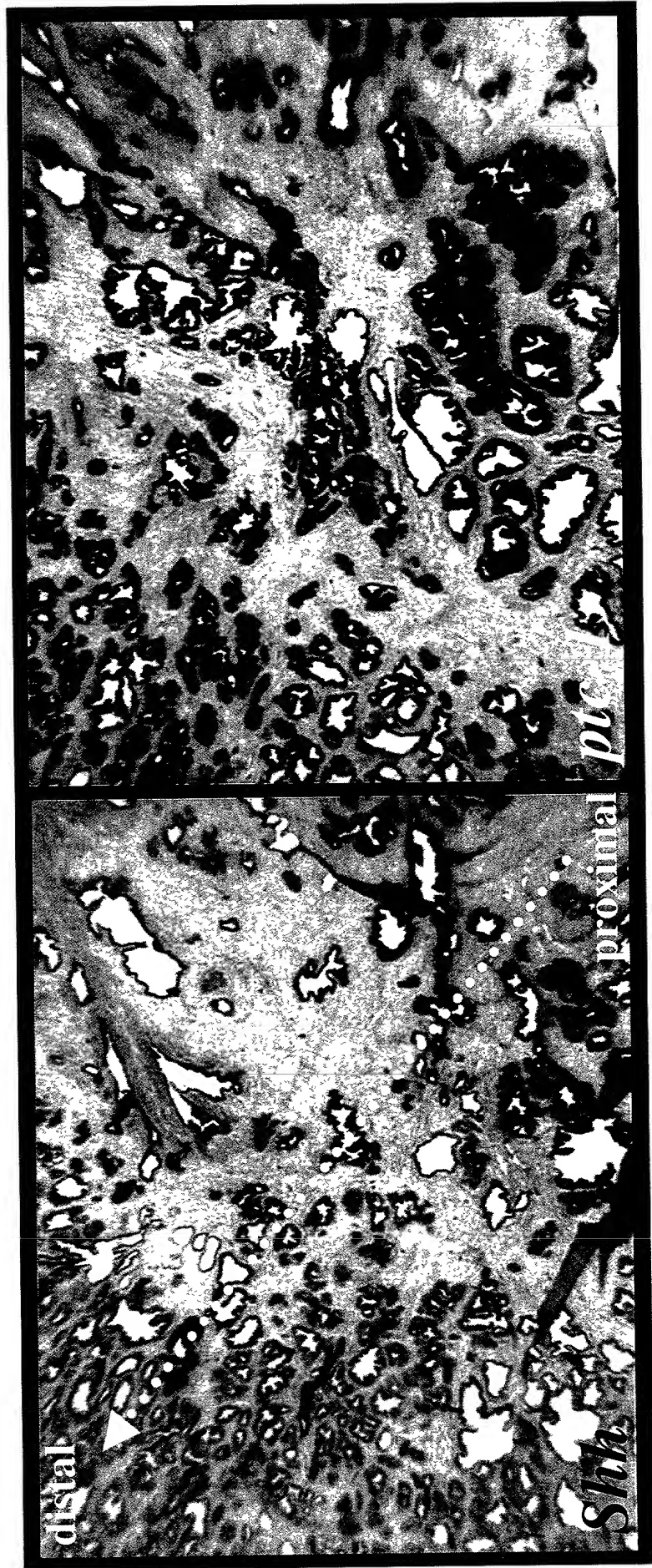


Fig. 33

# Hedgehog Signaling in BPH by Q-RT-PCR

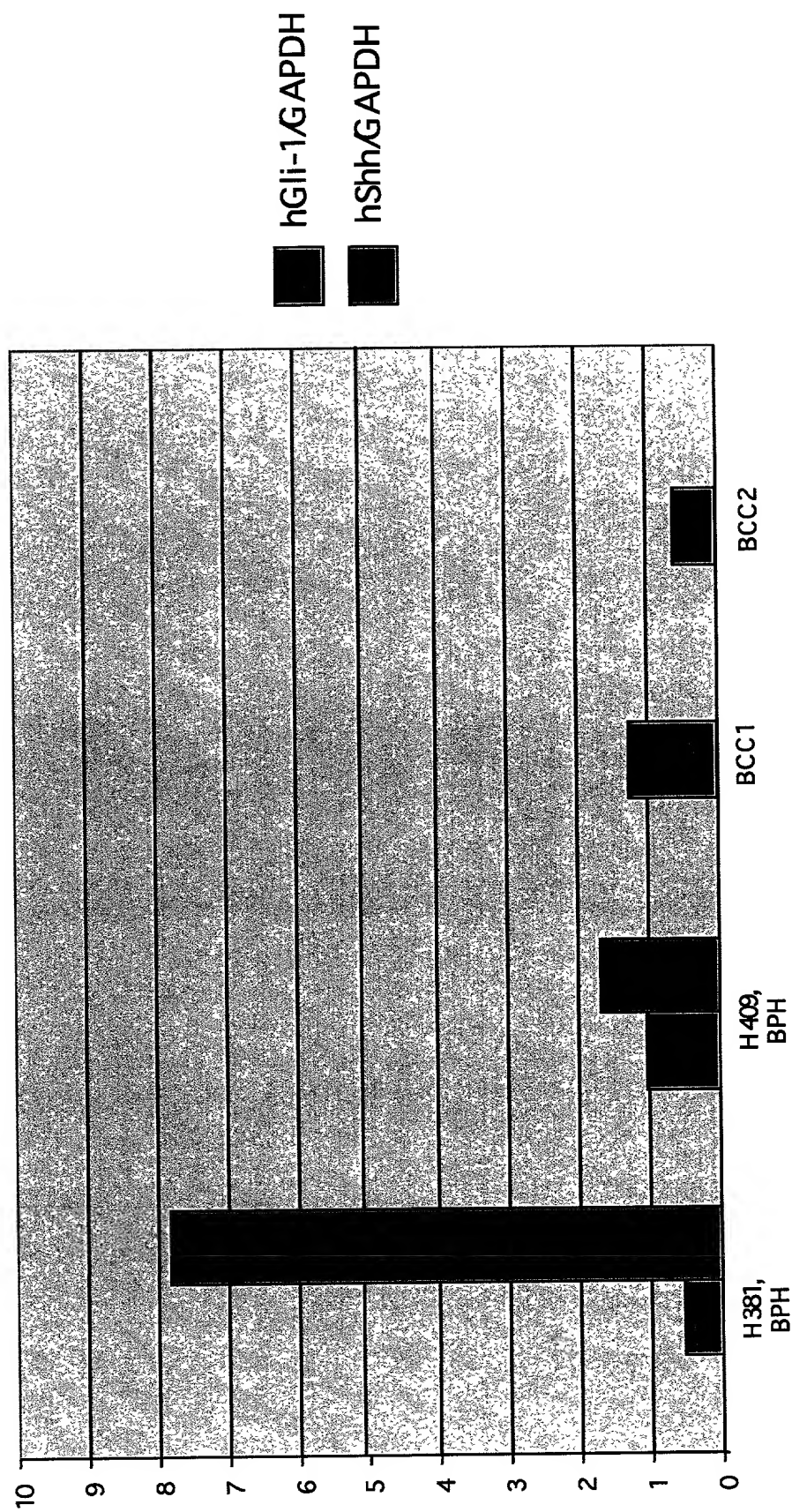
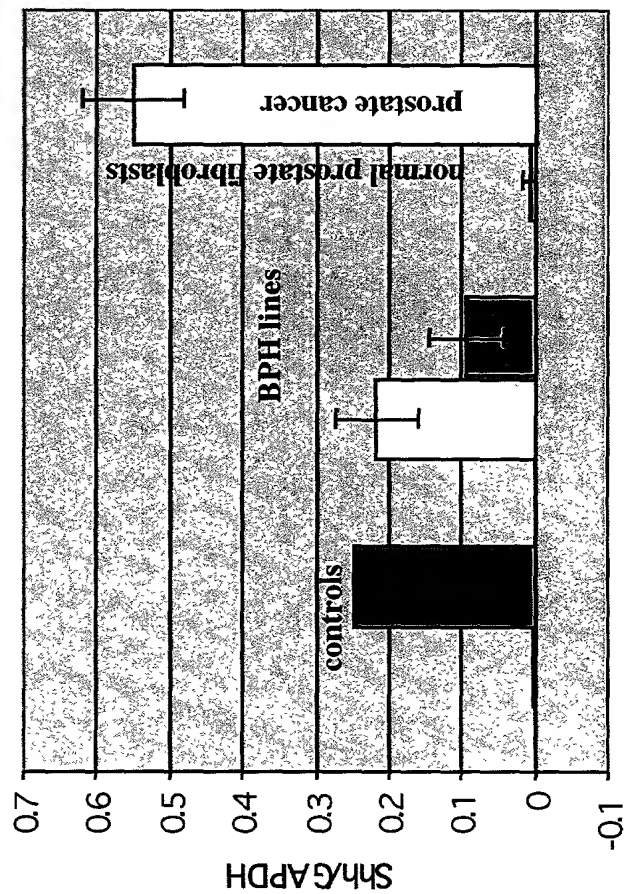


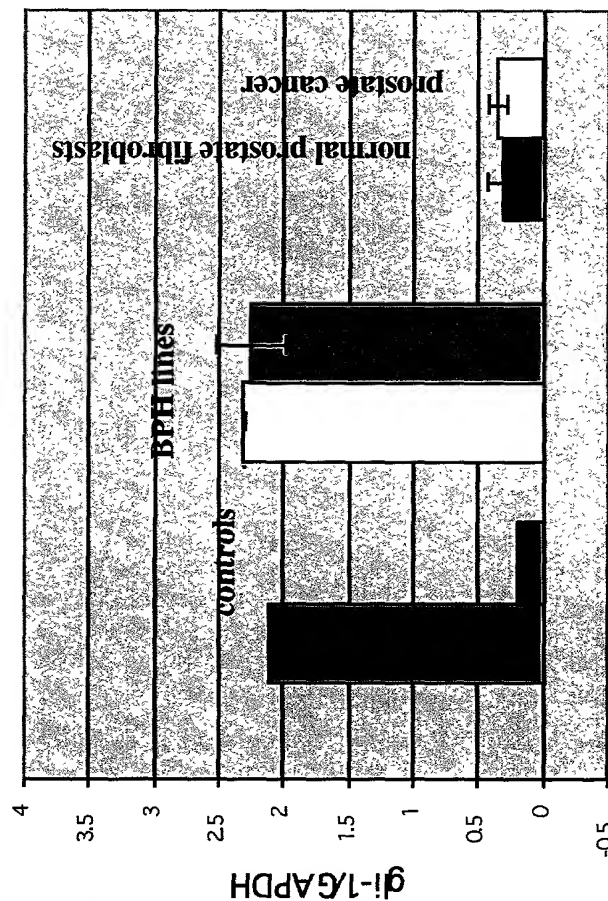
Fig. 34

# HIGH LEVEL HEDGEHOG SIGNALING IN BPH CELL LINES

*Shh*



*Gli-1*



- BCC
- fetal brain
- BRFF-55T (BPH)
- 267B (BPH)
- PrSc fibroblasts
- PC-3 (prostate cancer)

Fig. 35



FOST-19822650

## Effect of 5E1 on HT-29/10T1/2 Colon Cancer Growth

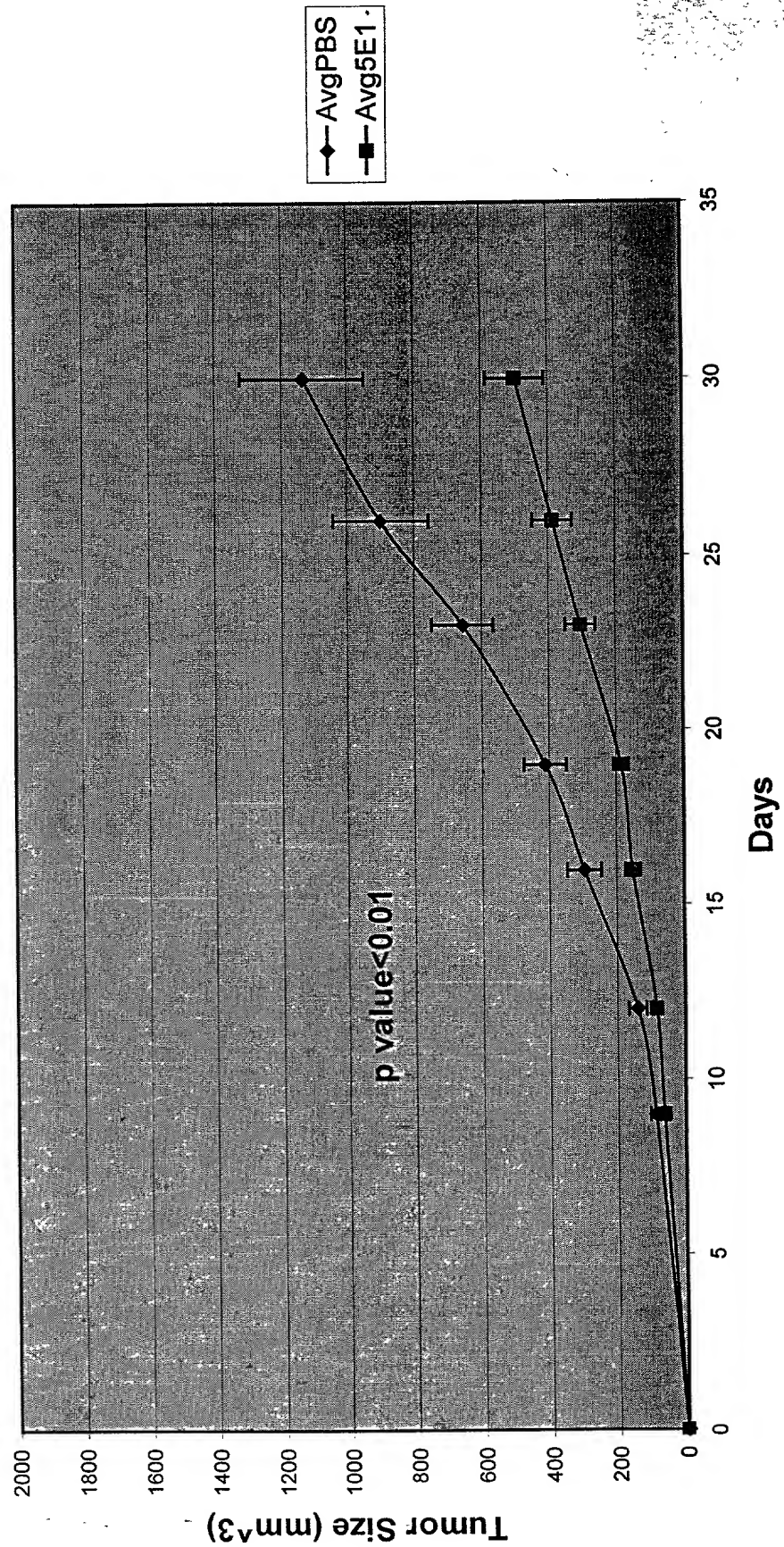


Fig. 36

## Effect of 5E1 on HT-29/10T1/2 Colon Cancer Growth

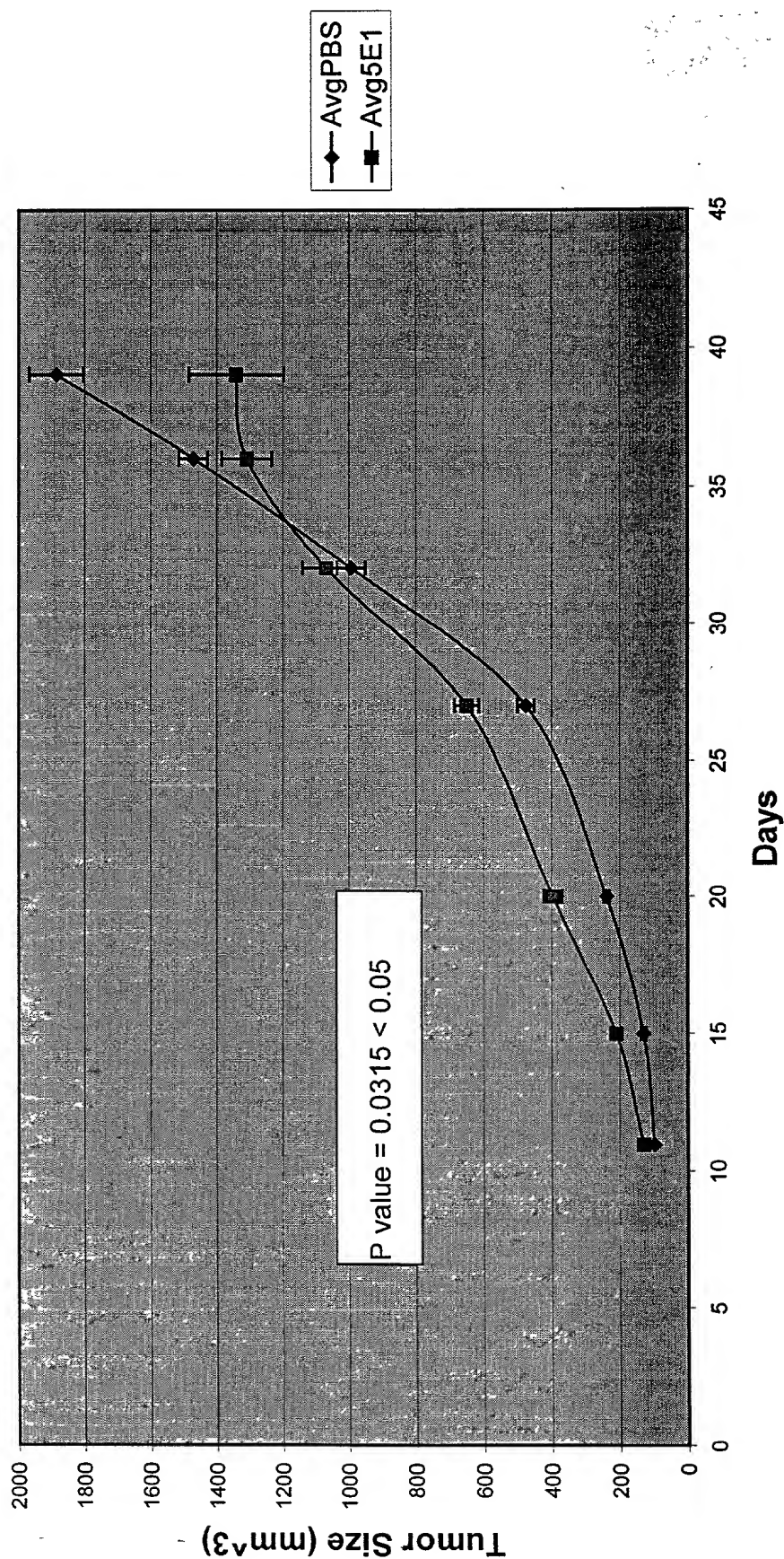


Fig. 37